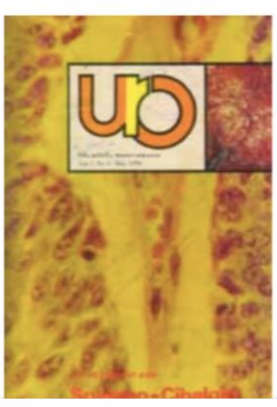
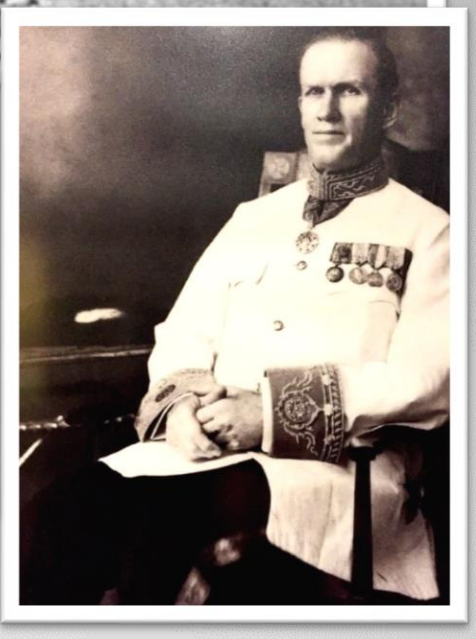
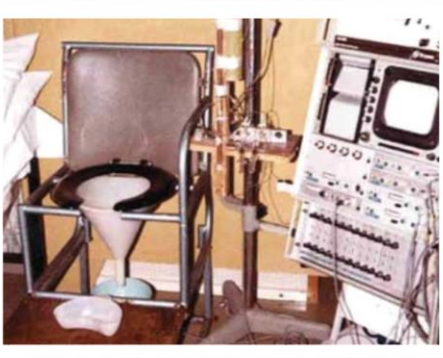
Insight UROLOGY

Volume 44 No. 1 Jan - June 2023







Official Journal of the Thai Urological Association under the Royal Patronage

www.tci-thaijo.org/index.php/TJU

ISSN 2730-3217 (Online) DOI:10.25786/isu.i.6

Insight UROLOGY
ISSN 2730-3217 (Online)

Official Journal of the Thai Urological Association under the Royal Patronage

Journal Policies

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

Objectives

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

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

Owner The Thai Urological Association under the Royal Patronage (TUA)

Office Division of Urology, Department of Surgery, Faculty of Medicine
Chiang Mai University, Muang, Chiang Mai, Thailand 50200
Tel: +66 5393-4535, +66 81288-3007 Fax: +66 5393-6139
E-mail: insighturology@gmail.com

Date of Issue Semi-annually (June and December)

Editorial

The fifth issue of *Insight Urology* (ISU) was published online in June 2023. It is composed of five original articles and two review articles. It covers several fields of urology, namely oncologic urology, endourology, and andrology.

Two review articles were submitted by renowned international authors: "**Review of various surgical approaches for varicocele management**" and "**Retroperitoneal lymph node dissection: the past, present, and future, a review**". We are sure that you will enjoy reading and applying the articles' contents to your present urological work, especially when treating varicocele in adult patients and performing complex surgery for testicular cancer.

The front cover of this issue features five photographs of important people, places, and items in the history of Thai Urology. The first photograph is of **Siriraj Hospital**, the first hospital in Thailand, which was founded by King Chulalongkorn in 1888. The second is of **Phra Ach Vidayagama**, the surgeon who performed the first suprapubic cystolithotomy in Thailand in 1892, while the third photograph is of **Dr. Samai Chanthawimol**, the first certified urologist of Thailand in 1964 and the first President of the Urology Society of Thailand. The fourth is of the first issue of the **Thai Journal of Urology**, which was released on May 1, 1976, and the fifth and final photograph is of one of the first **Uroflowmetry** Machines in Thailand, a crucial tool in Functional Urology which arrived in 1981.

The Editorial Board of ISU hopes that the cover of this issue will represent the beginnings and fundamentals of Thai Urology. Just as an African proverb states that "**If we stand tall it is because we stand on the shoulders of many ancestors**," we sincerely believe that a sophisticated future for Thai Urology requires the remembrance of our urological roots. Therefore, commemorating our history is crucial for stepping into the future.

No reserve. No retreat. No regret.

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

Contents

Original Article

Association between the levels of postoperative pyuria and urinary tract infection in patients undergoing Transurethral Anatomical Enucleation of Prostate (TUAEP) in Rajavithi Hospital

Jirapong Sa-nguancharoenpong, Tanet Thaidumrong

Division of Urology, Department of Surgery, Rajavithi Hospital, Bangkok, Thailand

Keywords:
Prostatic hyperplasia, Transurethral Anatomical Enucleation of Prostate, TUAEP, postoperative bacteriuria, postoperative pyuria

Abstract

Objective: Pyuria is a common condition that can occur after TUAEP. One possible cause is postoperative inflammation. To limit this many physicians prescribe antibiotic prophylaxis to prevent postoperative urinary tract infections, however this can lead to the overuse of antibiotics and increase the growing problem of antibiotic resistance. Therefore the object of this study is to evaluate the association between the level of postoperative pyuria and urinary tract infections in patients undergoing TUAEP and to identify other risk factors associated with postoperative urinary tract infection facilitating appropriate antibiotic management.

Materials and Methods: Data from 94 patients who underwent TUAEP in Rajavithi Hospital from 1st December 2016 to 31st March 2021 were retrospectively analyzed. The data collected from medical records included demographic data, details from operative record sheets and laboratory results.

Results: A significant association was found between a level of postoperative pyuria >100 WBCs/HPF and postoperative bacteriuria (46.15% vs 19.35%, p = 0.024). Diabetes mellitus and preoperative bacteriuria were also significant risk factors for postoperative bacteriuria. The bacterium which was the most frequently cultured from samples taken both preoperatively and postoperatively was *Escherichia coli*.

Conclusion: The risk factors for postoperative bacteriuria in patients undergoing TUAEP are a level of postoperative pyuria > 100/HPF, diabetes mellitus and preoperative bacteriuria. It may be concluded from the results that the most frequent cause of postoperative pyuria was more likely to be due to a tissue reaction after surgery than from a urinary tract infection. Selective antibiotic treatment in patients who have these risk factors can reduce problems of antibiotic overuse and antibiotic resistance.

Insight Urol 2023;44(1):1-6. doi: 10.52786/isu.a.65

Corresponding author: Tanet Thaidumrong
Address: Division of Urology, Department of Surgery, Rajavithi Hospital, Bangkok 10400, Thailand
E-mail: tncclinic@gmail.com
Manuscript received: April 12, 2022
Revision received: October 20, 2022
Accepted after revision: February 10, 2023

Introduction

The gold standard surgical treatment for patients with benign prostatic hyperplasia is transurethral resection of prostate (TURP) because of its excellent record of long-term efficacy.[1] However, it has some limitations, especially when prostate size is over 80 ml,[2] for example bleeding and TURP syndrome especially in the monopolar type.[3] Transurethral Anatomical Enucleation of Prostate (TUAEP)[4-6] is a technique which was developed from Transurethral Enucleation and resection of prostate (TUERP) by using a bipolar system for enucleation of the prostatic gland and using a morcellator to remove all lobes of the prostate gland floating in the urinary bladder. From the first pilot study in Thailand6, which was conducted in Rajavithi Hospital, it was shown that TUAEP was more advantageous with regard to reduction of bleeding and TURP syndrome when compared with M-TURP and more obstructing adenomas were removed in comparison to Bipolar-TURP (B-TURP). Thus, TUAEP has been established as an alternative to TURP especially when patients have a particularly enlarged prostate gland.[7,8]

Postoperative pyuria is commonly found after TUAEP. Its cause may be due to a tissue reaction after bipolar therapy rather than as a result of urinary tract infection.[9,10] The potential problem is that many physicians prescribe antibiotic prophylaxis when a urine culture has not been carried out to prevent postoperative urinary tract infections which can lead to the overuse of antibiotics and antibiotic resistance.[11,12] The aim of this study is to evaluate the association between the level of postoperative pyuria and urinary tract infections in patients undergoing TUAEP and also to identify other risk factors associated with postoperative urinary tract infections to inform appropriate antibiotic management and to investigate the most common bacterial strains found in preoperative and postoperative bacteriuria in patients undergoing TUAEP in Rajavithi Hospital.

Materials and Methods

Data from all 94 patients who underwent TUAEP in Rajavithi Hospital from 1st December 2016 to 31st March 2021 were retrospectively analyzed. The data were collected from medical records and included age, underlying diseases, medication, retention of the Foley catheter, preoperative and postoperative urine analysis and urine culture, PSA, operation time, weight of resected tissue, estimated blood loss, and tissue pathology. This research was approved by the Ethics Committee of Rajavithi Hospital (Study Number: 64120). Only 57 patients met the inclusion criteria, the other 37 patients being excluded due to the exclusion criteria, specifically, patients who were lost to follow-up including death, transfered back to another institution, no postoperative urine culture to confirm postoperative bacteriuria (> 105 CFU/ml)[13] and no postoperative pyuria (WBC > 5 cells/HPF).[14] Patient selection is shown in Figure 1.

The authors recorded and analyzed all data including age, underlying disease (diabetes mellitus), medication (5-ARIs), preoperative indwelling Foley catheter, PSA, length of operation, weight of resected tissue, estimated blood loss, tissue pathology, preoperative and postoperative urine analysis and urine culture. Data collection was followed up at 1, 2, 3, 6, and 12 months.

Data were analyzed using SPSS version 26.0 (SPSS Inc., Chicago, Illinois, USA). Baseline characteristics were analyzed using descriptive statistics, specifically number, percentage, mean and standard deviation, median, minimum and maximum. Chi-square or Fisher's Exact test were used to compare the categorical variables and frequency differences. The continuous data were analyzed using a student's T-test. A p-value of less than 0.05 was considered statistically significant.

Results

Patients were divided into postoperative urine culture positive and postoperative urine culture negative groups and these were compared against patient characteristics. The results are shown in Table 1. There were no significant differences in mean age (73.38±6.97 vs 70.06±7.94 years, p = 0.102), PSA median min-max (3.84 (1.83-43.52) vs 4.05 (0.97-21.1) ng/ml, p = 0.368), number of patients with preoperative retention of the Foley catheter (12 (46.15%) vs 7 (22.58%), p = 0.060), mean operative time (160.46±52.85 vs 141.84±40.81 minutes, p = 0.139), mean weight of resected tissue (43.09±22.29 vs 35.06±20.77 g, p = 0.165), mean estimated blood loss (310.38±49.27 vs 244.19±25.39 ml, p = 0.216) and number of patients with malignant pathology (2 (7.69%) vs 1 (3.23%), p = 0.587)

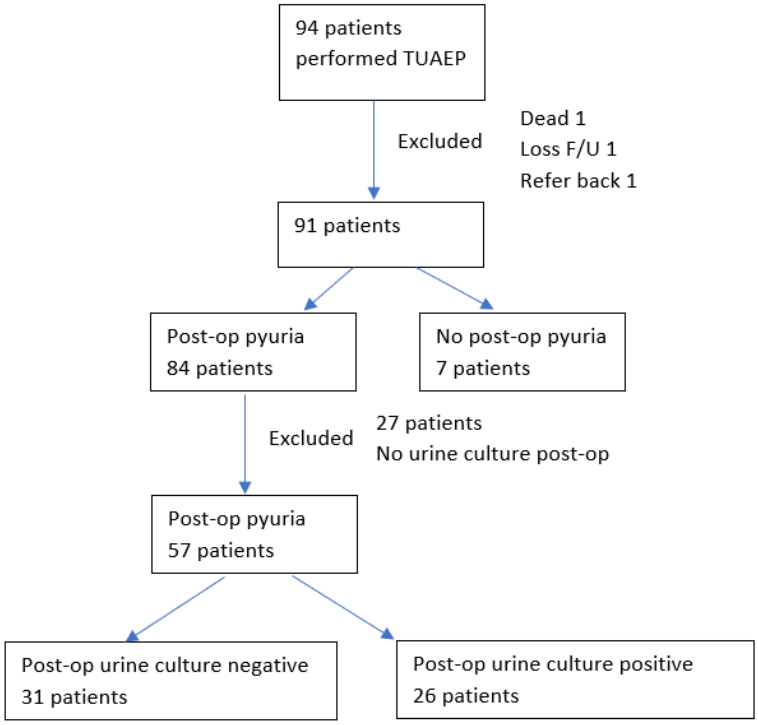


Figure 1. Study flow diagram showing the patient selection process

Table 1. Demographic data

Characteristic	Postoperative urine culture positive (n=26)	Postoperative urine culture negative (n=31)	P-value
Age (Mean±SD) (years) n (SD)	73.38±6.97	70.06±7.94	0.102
Diabetes mellitus n (%)	16 (61.54)	8 (25.81)	0.006
Preoperative bacteriuria n (%)	12 (46.15)	5 (16.13)	0.014
PSA median (min-max)	3.84 (1.83-43.52)	4.05 (0.97-21.1)	0.368
On 5-ARIs n (%)	5 (19.23)	14 (45.16)	0.039
On Foley catheter n (%)	12 (46.15)	7 (22.58)	0.060
Operation time (minutes) n (SD)	160.46±52.85	141.84±40.81	0.139
Weight of resected tissue (g) n (SD)	43.09±22.29	35.06±20.77	0.165
Estimated blood loss (ml) n (SD)	310.38±49.27	244.19±25.39	0.216
Malignant pathology n (%)	2 (7.69)	1 (3.23)	0.587

Significant p-value < 0.05

Diabetic mellitus (16 (61.54%) vs 8 (25.81%), p = 0.006) and preoperative bacteriuria (12 (46.15%) vs 5 (16.13%), p = 0.014) were the statistically significant risk factors for postoperative bacteriuria. Patients who had taken 5-ARIs preoperatively showed a statistically significant lower level of postoperative bacteriuria (5 (19.23%) vs 14 (45.16%), p = 0.039).

The correlation between the level of postoperative pyuria and bacteriuria is shown in Table 2. A significant association was found between the level of postoperative pyuria > 100 WBCs/HPF and postoperative bacteriuria compared with the group with a negative postoperative urine culture (12 (46.15%) vs 6 (19.35%), p = 0.024). The level of postoperative pyuria between 50-100 WBCs/HFP was not significantly different between the groups with a positive and negative postoperative urine culture (4 (15.38%) vs 3 (9.68%), p = 0.691). The level of postoperative pyuria < 50 WBCs/HPF was significantly lower in the group with a postoperative positive urine culture (10 (38.46%) vs 22 (70.97%), p = 0.014).

Table 2. Correlation between the level of postoperative pyuria and bacteriuria

Level of postoperative pyuria (WBC/HPF)	Postoperative urine culture positive (n=26) n (%)	Postoperative urine culture negative (n=31) n (%)	P-value
> 100	12 (46.15)	6 (19.35)	0.024
50-100	4 (15.38)	3 (9.68)	0.691
< 50	10 (38.46)	22 (70.97)	0.014

Significant p-value < 0.05

Table 3. Bacterial spectrum in patients with preoperative bacteriuria

Bacterial strains	Number of patients (n=17) n (%)
Escherichia coli	8 (47.06)
Escherichia coli ESBL	4 (23.53)
Enterococcus faecalis	3 (17.65)
Staphylococcus haemolyticus	1 (5.88)
Klebsiella pneumoniae	1 (5.88)

Table 4. Bacterial spectrum in patients with postoperative bacteriuria

Bacterial strains	Number of patients (n=26) n (%)
Escherichia coli	9 (34.62)
Enterococcus faecalis	6 (23.08)
Escherichia coli ESBL	5 (19.23)
Klebsiella pneumoniae	2 (7.69)
Klebsiella pneumoniae ESBL	1 (3.85)
Staphylococcus haemolyticus	1 (3.85)
Acinetobacter baumannii	1 (3.85)
Corynebacterium	1 (3.85)

The spectra of preoperative bacteriuria are shown in Table 3, and spectra of postoperative bacteriuria are shown in Table 4. Preoperatively, *Escherichia coli* (47.06%) was the most frequently cultured bacteria, the second was *Escherichia coli* ESBL (23.53%), and the third was Enterococcus faecalis (17.65%). Postoperatively, *Escherichia coli* was still the most frequently cultured bacteria (34.62%), whereas the second was Enterococcus faecalis (23.08%), and the third was *Escherichia coli* ESBL (19.23%).

The duration of postoperative pyuria is shown in Table 5. The most frequent duration is 2 months (23 patients, 43.86%) followed by 3 months (17, 29.82%), 1 month (7, 12.28%), 6 months (5, 8.77%), and 12 months (3, 5.26%).

Table 5. Duration of postoperative pyuria

Duration of postoperative pyuria (months)	Number of patients (n=57) n (%)
1	7 (12.28)
2	25 (43.86)
3	17 (29.82)
6	5 (8.77)
12	3 (5.26)

Discussion

Postoperative pyuria was commonly found after TUAEP,[15] including 92.31% of patients in this study, but postoperative bacteriuria was only found in 45.61% of cases. Prior to this study physicians did not wait for urine culture results and many prescribed antibiotic prophylaxis to prevent postoperative urinary tract infections. This practice can lead to the overuse of antibiotics and antibiotic resistance. The significant risk factors associated with postoperative bacteriuria (p-value < 0.05) were a level of postoperative pyuria > 100 WBCs/HPF, diabetic mellitus and preoperative bacteriuria. Selective antibiotic treatment solely in this group of patients could reduce the significant problems of overuse and antibiotic resistance.

Patients with levels of postoperative pyuria < 50 WBCs/HPF were significantly associated with the group of negative postoperative bacteriuria and antibiotic treatment can be omitted if the patients don't have any other risk factors or clinical symptoms. Postoperative pyuria with a level of 50-100 WBCs/HPF is the grey zone because

there was no difference between the two groups. Antibiotic prophylaxis may be considered in diabetic patients or patients who have preoperative bacteriuria.[16] The possibility that 5-alpha reductase inhibitors (5-ARIs) can reduce the rate of postoperative bacteriuria has been suggested. This may be due to 5- ARI treatment reducing the rate of prostatic vascularity, and decreasing perioperative bleeding. The most frequently cultured bacterium, both preoperatively and postoperatively, was *Escherichia coli*. Therefore an antibiotic that covers gram-negative bacterial strains is suggested. Postoperative pyuria was resolved in most patients within 3 months (85.96%).

One limitation to this study is that is was retrospective in nature and therefore is subject to variations in collection and surgical techniques and a second is that due to the large number of exclusions the sample size was quite small. In the future, a prospective study with a larger number of participants is warranted to verify and identify other significant risk factors and improve statistical outcomes.

Conclusion

The risk factors for postoperative bacteriuria in patients undergoing TUAEP are a level of postoperative pyuria > 100 WBCs/HPF, a comorbidity of diabetic mellitus and preoperative bacteriuria. It may be concluded from the results that the majority of causes of postoperative pyuria came from tissue reaction after surgery rather than from urinary tract infections. Selective antibiotic treatment for patients who have these specific risk factors can reduce the problems of antibiotic overuse and antibiotic resistance. Preoperative 5-ARIs may be considered as an option for reducing postoperative bacteriuria.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. Reich O, Gratzke C, Stief CG. Techniques and longterm results of surgical procedures for BPH. Eur Urol 2006;49:970-8.
2. Helo S, Welliver Jr RC, McVary KT. Minimally Invasive and Endoscopic Management of Benign Prostatic Hyperplasia. In: Partin AW, Dmochowski RR, Kavoussi LR, Peters CA, editors. Campbell-Walsh-Wein Urology. 12th ed. Philadelphia: Elsevier; 2020. p. 3437.
3. Mebust WK, Holtgrewe HL, Cockett AT, Peters PC. Transurethral prostatectomy: immediate and postoperative complications. A cooperative study of 13 participating institutions evaluating 3,885 patients. J Urol 1989;141:243-7.
4. Eaton AC, Francis RN. The provision of transurethral prostatectomy on a day-case basis using bipolar plasma kinetic technology. BJU Int 2002;89:534-7.
5. Botto H, Lebret T, Barre P, Orsoni JL, Herve JM, Lugagne PM. Electrovaporization of the prostate with the Gyrus device. J Endourol 2001;15:313-6.
6. Thaidumrong T, Duangkae S, Jiramanee V, Kalapong J, Pisansalhidikam P. Transurethral Anatomical Enucleation of Prostate (TUAEP) in Benign Prostatic Hyperplasia with Bipolar system : First study in Thailand. J Med Assoc Thai 2019;102:20-5.
7. Tuhkanen K, Heino A, Ala-Opas M. Two-year followup results of a prospective randomized trial comparing hybrid laser prostatectomy with TURP in the treatment of big benign prostates. Scand J Urol Nephrol 2001;35:200-4.
8. Souverein PC, van Riemsdijk MM, de la Rosette JJ, Opdam PC, Leufkens HG. Treatment of benign prostatic hyperplasia and occurrence of prostatic surgery and acute urinary retention: a population-based cohort study in the Netherlands. Eur Urol 2005;47:505-10.
9. Liu C, Zheng S, Li H, Xu K. Transurethral enucleation and resection of prostate in patients with benign prostatic hyperplasia by plasma kinetics. J Urol 2010;184:2440-5.
10. Neill MG, Gilling PJ, Kennett KM, Frampton CM, Westenberg AM, Fraundorfer MR, et al. Randomized trial comparing holmium laser enucleation of prostate with plasmakinetic enucleation of prostate for treatment of benign prostatic hyperplasia. Urology 2006;68:1020-4.
11. Yoshikazu T, Koji F, Yasuo U, Sojun K, Yosuke S, Koichiro W, et al. Comparison of single- and multiple-dose cefazolin as prophylaxis for transurethral enucleation of prostate: A multicenter, prospective, randomized controlled trial by the Japanese Research Group for Urinary Tract Infection. Int J Urol 2020; 27:244-8.
12. Xiong W, Sun M, Ran Q, Chen F, Du Y, Dou K. Learning curve for bipolar transurethral enucleation and resection of the prostate in saline for symptomatic benign prostatic hyperplasia: experience in the first 100 consecutive patients. Urol Int 2013;90:68-74.
13. Roehrborn CG, Strand DW. Benign Prostatic Hyperplasia: Etiology, Pathophysiology, Epidemiology, and Natural History. In: Partin AW, Dmochowski RR, Kavoussi LR, Peters CA, editors. Campbell-Walsh-Wein Urology. 12th ed. Philadelphia: Elsevier; 2020.

p. 3305.
14. Cooper KL, Badalato GM, Rutman MP. Infection of the Urinary Tract. In: Partin AW, Dmochowski RR, Kavoussi LR, Peters CA, editors. Campbell-Walsh-Wein Urology. 12th ed. Philadelphia: Elsevier; 2020. p. 1129.
15. Zhang KY, Xing JC, Chen BS, Liu CX, Lau HW, Sim HG, et al. Bipolar plasmakinetic transurethral resection of the prostate vs. transurethral enucleation and resection of the prostate: pre-and postoperative comparisons of parameters used in assessing benign prostatic enlargement. Singapore Med J 2011;52:747-51.
16. Nicolle LE, Bradley S, Colgan R, Rice JC, Schaeffer A, Hooton TM, et al. Infectious diseases society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. Clin Infect Dis 2005;40:643-54.

Original Article

Comparison of the results of bipolar transurethral enucleation and resection of the prostate with and without morcellation in treatment of benign prostatic hyperplasia

Thatree Weerasawin

Department of Surgery, Lampang Hospital, Lampang, Thailand

Keywords:
Benign prostatic hyperplasia, bipolar transurethral enucleation and resection of the prostate, morcellation

Abstract

Objective: To compare the result of bipolar transurethral enucleation and resection of the prostate with morcellation (B-TUERP-M) and without morcellation (B-TUERP) in treatment of benign prostatic hyperplasia.

Materials and Methods: This was a prospective single centre cohort study of 101 patients with prostate enlargement of more than 60 ml who underwent B-TUERP by a single surgeon between January 2020 and June 2022. Patients were divided into two groups, a B-TUERP group of 49 patients and a second group of 52 patients classed as B-TUERP-M. The perioperative outcomes followed up at 1, 3 and 6 months after surgery were evaluated.

Results: There were no significant differences in the preoperative parameters of the two groups. Comparisons between the two groups showed a shorter operative time (63.94 ± 12.01 vs 77.77 ± 11.80 min, p-value 0.000), more resected prostate tissue (65.73 ± 14.67 vs 60.73 ± 5.45 gm, p-value 0.027) and a higher post-operative hematocrit level (35.16 ± 3.97 vs 33.18 ± 3.22%, p-value 0.007) in the patients who underwent B-TUERP with morcellation. At 6 months after the procedure, better results were found in patients who had undergone B-TUERP-M regarding urine flow rate (26.33 ± 5.33 vs 20.66 ± 5.08 ml/sec, p-value 0.000), post-void residual urine volume (24.19 ± 10.93 vs 36.04 ± 16.90 ml, p-value 0.000), post-operative PSA (0.72 ± 0.43 vs 1.22 ± 0.54 mg/ml, p-value 0.000) and International Prostate Symptom Scores (5.01 ± 1.36 vs 5.71 ± 1.33, p-value 0.001).

Conclusion: Better outcomes occurred following B-TUERP with morcellation with regard to operative time, resection weight of prostatic adenoma, post-operative urine flow rate, Post-void residual urine volume, PSA and International Prostate Symptom Score than in patients treated with B-TUERP without morcellation.

Insight Urol 2023;44(1):7-13. doi: 10.52786/isu.a.66

Corresponding author: Thatree Weerasawin
Address: Department of surgery, Lampang Hospital, 280 Paholyothin Road, Muang, Lampang 52000, Thailand
E-mail: Superjumboaw@gmail.com
Manuscript received: February 17, 2023
Revision received: April 27, 2023
Accepted after revision: May 13, 2023

Introduction

The first monopolar transurethral resection of the prostate (M-TURP) was introduced in 1963 by Maximilian Sterm and remains the gold standard for surgical treatment of benign prostatic hyperplasia (BPH)[1] but still has some limitations, especially when prostate size is over 80 ml.[2,3] BPH can result in bleeding and transurethral resection of prostate (TURP) syndrome[4,5] with can cause serious complications. The bipolar TURP (B-TURP) was introduced to reduce the risk of TURP syndrome by using saline as the irrigation fluid but this does not reduce the risk of intra-operative bleeding, especially in surgery involving a large prostate gland.[6] Currently, there is increasing use of the technique known as bipolar transurethral enucleation and resection of the prostate (B-TUERP) to enucleate the prostate adenomas in an endoscopic fashion. This technique removes more of the obstructing adenoma and the result is an effective and safe treatment of BPH.[7-9]

The extraction of adenoma of the prostate in a fragmentary fashion is a recognized practice. First, a loop electrode is used to resect the adenoma then all adenoma fragments are extracted using either an Ellic or Toomey syringe[8] with potential secondary use of the morcellator.[9] To our knowledge, there is no published data comparing these two techniques. This article aims to study the comparison of the results of bipolar transurethral enucleation and resection of the prostate without use of a morcellator (B-TUERP) and with use of a morcellator (B-TUERP-M).

Materials and Methods

The study was approved by the Research Ethics Committee of Lampang Hospital (study number: 80.1/64). A prospective cohort study was performed into 101 consecutive patients who were treated for benign prostatic hyperplasia using TUERP. The same surgeon carried out all the surgery between January 2020 and June 2022. Patients were divided into two groups: one group of 49 patients who underwent B-TUERP without morcellation and a second group, of 52 patients who underwent B-TUERP-with morcellation. The inclusion criteria were as follows: patients between 50 and 90 years of age, a prostate size of more than 60 ml measured using transrectal ultrasound and refractory to medical treatment. Exclusion criteria were diagnosis with a neurogenic bladder, prostate cancer, urethral stricture or any previous prostatic, bladder neck or urethral surgery. The author recorded and analyzed data including mean age, International Prostate Symptom Score, quality of life score, urine flow rate, post-void residual urine volume, PSA pre-operatively. Follow-up data from patients were collected 1, 3 and 6 months postoperatively.

The prostate volume, operative time, resection weight, catheterization time, pre and post-operative Hematocrit, percentage of blood transfusion and sepsis were also recorded. In the B-TUERP group, the author followed the technique described by LIU.[8] The procedure was performed in each case by a single surgeon with a 26 Fr resectoscope with bipolar loop. Normal saline served as the irrigation fluid. Under general or regional anesthesia, the patient was placed in the lithotomy position. The 26 Fr resectoscope was placed in the bladder under video assisted endosurgical system guidance. The ureteric orifice, bladder neck and verumontanum were identified. The incision was begun close to the verumontanum from the 5 to the 7 o'clock positions and the urethral mucosa was deeply incised to the level of the surgical capsule (Figure 1). The distal mid lobe and mucosa were dissected in retrograde fashion toward the bladder neck using the resectoscope tip combined with a loop. The loop was used to cut off the adenoma and adhesive fibers between the lobe and the surgical capsule at any time with the tip inserted into the previous cleavage to efficiently detach the adenoma along the capsule. Thus, adenoma of distal mid lobe was detached from the surgical capsule and the smooth surgical capsule was identified (Figure 2). The partial mid lobe was raised. The loop electrode was used to cauterize them and block the lobe blood supply (Figure 3). This procedure was used progressively towards the bladder neck until the circular fibers of the bladder neck were identified (Figure 4). The bilateral lobes along the surgical capsule were then detached clockwise or counterclockwise from the 5 or 7 o'clock position of the prostatic apex to the 12 o'clock position in the same direction. The loop electrode was used to cut from the 11 to 1 o'clock position (Figure 5) care being taken at the 12 o'clock position not to damage the external urethral sphincter. In a trilobe enlarge prostate the 3-lobe technique was used. This involved both

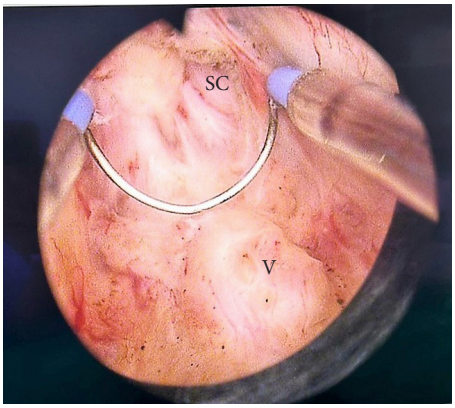


Figure 1. The incision was begun close to the verumontanum (V) from the 5 to the 7 o'clock positions and a deep incision was made in the urethral mucosa to the level of the surgical capsule (SC).

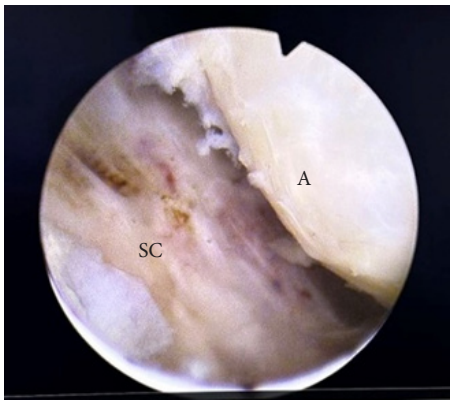


Figure 2. The adenoma (A) was detached from the surgical capsule and the smooth surgical capsule (SC) was identified.

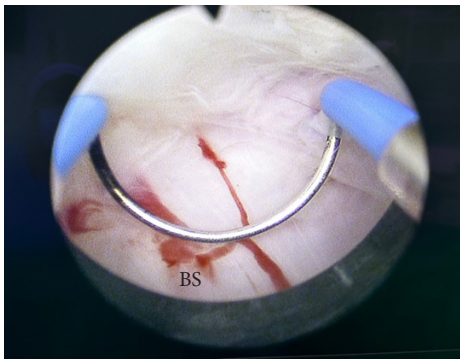


Figure 3. The loop electrode was used to cauterize them and block the lobe blood supply (BS).

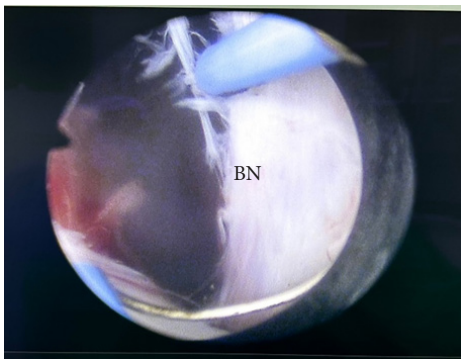


Figure 4. The circular fibers of the bladder neck (BN) were identified.

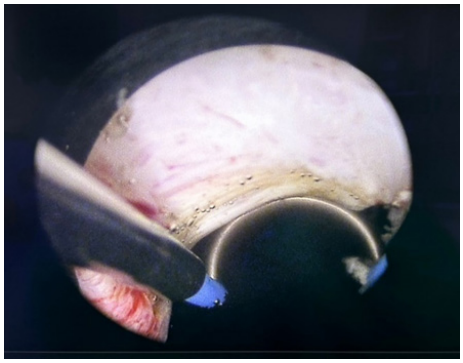


Figure 5. The loop electrode was used to cut from 11 to 1 o'clock position.

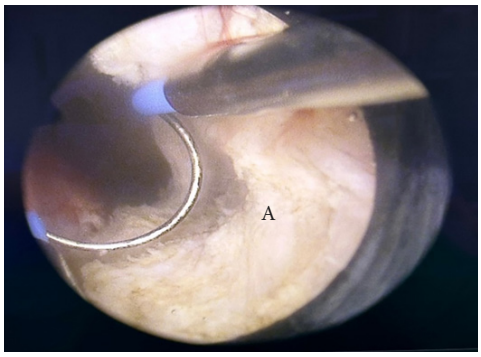


Figure 6. The adenoma(A) was resected rapidly by the loop electrode without serious hemorrhage.

a 5 and 7 o'clock incision with median lobe enucleation and subsequent enucleation of the bilateral lobe with the technique described. At this point, all the lobes of prostate attached to the bladder neck and most of the blood supply to the lobes were blocked. The adenoma was resected rapidly using the loop electrode without incidence of serious hemorrhage (Figure 6). All adenoma fragments were extracted by Toomey syringe. A 22 Fr 3-way catheter was inserted. Bladder irrigation was necessary until hematuria was sufficiently resolved. In the B-TUERP-M group, the author followed the technique described by Thaidumrong.[9] Equipment and the techniques used for enucleation of all lobes of the prostate are identical to those used in the B-TUERP group. When all lobes were detached from the surgical capsule, the loop electrode was used to cut the point of attachment on the bladder neck to free the adenoma. The tip of resectoscope was used to

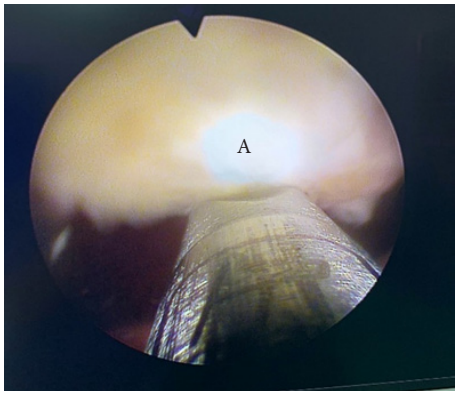


Figure 7. All adenomas(A) were pushed to float into the bladder.

push all adenomas to cause them to float into the bladder (Figure 7). In the final step, a morcellator was used to remove the floating adenoma from the bladder. A 22 Fr 3-way catheter was inserted. Bladder irrigation was necessary until hematuria was sufficiently resolved.

Statistical analysis

The data were analyzed using Stata/SE17. The data are presented as mean ± standard deviation (SD) and percentages. The perioperative and postoperative data between the B-TUERP and B-TUERP-M groups was compared via independent t-test. A p-value of less than 0.05 was considered statistically significant.

Results

Table 1 represents the baseline preoperative parameters of the patients fitting the inclusion criteria. There was no statistical difference between the two groups regarding preoperative parameters; both groups had comparable preoperative values regarding age, IPSS, QOL, PVR, Pre-test PSA, prostate volume, and pre-test hematocrit.

Table 2 represents the perioperative parameters in the two groups. The perioperative data showed significant differences between the groups with regard to operative time, which was longer in the B-TUERP group than in the B-TUERP-M group (77.77 ± 11.80 vs 63.94 ± 12.01 min, p-value 0.000); the tissue resection weight was significantly less in the B-TUERP group in relation the B-TUERP-M group (60.73 ± 5.45 vs 65.73 ± 14.67 gm, p-value 0.027), and the post-operative hematocrit was significant lower in the B-TUERP group than in the B-TUERP-M group (33.18 ± 3.22 vs 35.16 ± 3.97%, p-value 0.007). However, there were no statistical differences between the two groups in catheterization time, post-operative sepsis and blood transfusion.

Table 3 shows the outcomes. With regard to the post-operative parameters, there were

Table 1. Baseline preoperative parameters of the included patients

Variables	B-TUERP group (n=49) Mean ±SD	B-TUERP-M group (n=52) Mean ±SD	P-value
Age (year)	72.30±7.26	70.01±7.31	0.124
IPSS	22.12±2.55	22.03±1.57	0.878
QOL	4.63±0.65	4.42±0.50	0.175
Qmax (ml/sec)	6.81±1.66	7.11±1.57	0.475
PVR (ml)	147.15±37.46	148.5±26.57	0.873
Pre-test PSA	4.86±1.15	4.85±1.21	0.975
PV (ml)	80.10±10.50	81.90±16.09	0.508
Pre-test Hct	37.77±3.54	38.80±3.88	0.166

B-TUERP-M = Bipolar transurethral enucleation and resection of the prostate with morcellator, IPSS = International Prostate Symptom Score, QOL = quality of life score, Qmax = urine flow rate, PVR = post-void volume residual urine, PSA = prostate specific antigen, PV = prostate volume

Table 2. Perioperative parameters in the two groups

Variables	B-TUERP group (n=49) Mean ±SD	B-TUERP-M group (n=52) Mean ±SD	P-value
Operative time (min)	77.77±11.80	63.94±12.01	0.000
Resection weight (gm)	60.73±5.45	65.73±14.67	0.027
Catheterization time (day)	2.42±0.95	2.25±0.86	0.326
post-operative Hct (%)	33.18±3.22	35.16±3.97	0.007
post-operative sepsis (%)	3 (5.7)	2 (3.8)	0.659
Blood transfusion n (%)	9 (17.0)	4 (7.7)	0.096

Table 3. Post-operative parameters in the two groups

Variables	B-TUERP group (n=49) Mean ±SD	B-TUERP-M group (n=52) Mean ±SD	P-value
Postoperative Q max (ml/sec)			
1 month	15.21±3.65	22.02±5.60	0.000
3 months	18.49±4.49	24.89±5.98	0.000
6 months	20.66±5.08	26.33±5.33	0.000
Postoperative PVR (ml)			
1 month	62.67±24.29	32.42±19.81	0.000
3 months	50.26±19.97	27.51±14.49	0.000
6 months	36.04±16.90	24.19±10.93	0.000
Postoperative PSA (ng/ml)			
1 month	1.84±0.73	1.08±0.73	0.000
3 months	1.43±0.60	0.85±0.47	0.000
6 months	1.22±0.54	0.72±0.43	0.000
Postoperative IPSS			
1 month	10.59±1.98	10.34±1.73	0.509
3 months	7.67±1.57	7.38±1.34	0.322
6 months	5.71±1.33	5.01±1.36	0.001
Postoperative QOL			
1 month	2.48±0.68	2.38±0.63	0.422
3 months	1.61±0.57	1.46±0.54	0.176
6 months	0.97±0.43	0.88±0.37	0.242

B-TUERP-M = Bipolar transurethral enucleation and resection of the prostate with morcellator, Qmax = urine flow rate, PVR = post-void volume residual urine, PSA = prostate specific antigen, IPSS = International Prostate Symptom Score, QOL = quality of life score

significant differences between the groups in the post-operative Qmax values which were lower in the B-TUERP group than in the B-TUERP-M group at 1, 3 and 6 months (15.21 ± 3.65 vs 22.02 ± 5.60 ml/sec, p-value 0.000, 18.49 ± 4.49 vs 24.89 ± 5.98 ml/sec, p-value 0.000 and 20.66 ± 5.08 vs 26.33 ± 5.33 ml/sec, p-value 0.000). The post-operative PVR was higher in the B-TUERP group than in the B-TUERP-M group at 1, 3 and 6 months (62.67 ± 24.29 vs 32.42 ± 19.81 ml, p-value 0.000, 50.26 ± 19.97 vs 27.51 ± 14.49 ml, p-value 0.000 and 36.04 ± 16.90 vs 24.19 ± 10.93 ml p-value 0.000). Post-operative PSA readings were higher in the B-TUERP group than in the B-TUERP-M group at 1, 3 and 6 months (1.84 ± 0.73 vs 1.08 ± 0.73 ng/ml, p-value0.000, 1.43 ± 0.60 vs 0.85 ± 0.47 ng-ml, p-value 0.000 and 1.22 ± 0.54 vs 0.72 ± 0.43 ng/ml, p-value 0.000). Also, the post-operative IPSS was higher in the B-TUERP group than the B-TUERP-M group at 6 months (5.71 ± 1.33 vs 5.01 ± 1.36, p-value 0.001). There was no significant difference between the two groups in post-operative IPSS at 1 and 3 month follow ups and post-operative QOL at 1, 3 and 6 months.

Discussion

BPH is a common disease in aging men, resulting in cumbersome lower urinary tract symptoms.[10] M-TURP is still the mainstream line of surgical management for relieving outlet obstruction in men with BPH. However, M-TURP is associated with a high complication rate ranging between 7% to 43% and a mortality rate of 0.2%.[11] The major complications are bleeding, TURP syndrome, extravasation and bladder neck stenosis.[9] The use of the B-TURP procedure can reduce the risk of TURP syndrome by using saline as the irrigation fluid but it does not reduce the risk of intraoperative bleeding especially in surgery involving an enlarged prostate gland.[6] The TUERP is a new surgical technique that replicates the open enucleation of prostate adenoma in an endoscopic fashion for treatment of BPH with a bipolar system. TUERP involves enucleation using the tip of a resectoscope in a similar fashion to index finger enucleation in open simple prostatectomy.[9] Neill et al, who first reported bipolar prostate enucleation, concluded that the technique was safe and technically feasible for BPH.[12] Subsequently, there have been many reports on the results of B-TUERP. Liu et al, have reported on the results of B-TUERP in 1,100 patients and suggest that TUERP is a safe, technically feasible treatment for BPH.[8] Davide et al, make a comparison between B-TUERP and B-TURP, carrying out an ESUT systematic review and cumulative analysis and they concluded that B-TUERP is an effective and safe surgical treatment for BPH. They went on to report that B-TUERP offers several advantages over standard B-TURP, including the resection of a larger amount of tissue within the same operative time, shorter hospitalization, lower risk of complications and a lower re-intervention rate.[13] Thaidumrong et al carried out a study in Thailand and reported on the results of TUAEP (the same technique as TUERP described by Liu with some modifications)[9] and used a morcellator to remove prostate adenoma from the bladder in 40 patients. They concluded that TUERP was potentially the best modern alternative to TURP and open prostatectomy for BPH.[9] However, the step involving a morcellator in TUERP after enucleation that can separate the prostate adenoma from the capsule of the prostate and remove the prostate adenoma from the bladder is not yet available. A loop electrode was used to resection the adenoma over and over to result in small fragments, which are removed using either an Ellic or Toomey syringe.[8] Later a morcellator was used to remove the prostate adenoma from the bladder. Julia et al reviewed 26 studies from 1998 to 2020 involving 5,652 patients treated with a morcellator for BPH. The team concluded that the morcellator is an efficient and safe for prostate morcellation in the TUERP technique.[14] To our knowledge, there is no published data comparing the results between using and not using a morcellator in TUERP. This article aimed to compare the results of the two techniques B-TUERP and B-TUERP-M. The perioperative parameters show that the B-TUERP-M group have a shorter operative time than the B-TUERP group (63.94 VS 77.77 min, p-value 0.000). The author found that use of the loop electrode in resection of the adenoma had a level of difficulty because of poor vision due to bleeding and obstruction of the equipment movement from prostate adenoma. To the contrary, use of a morcellator, after the adenoma has been pushed into the bladder facilitated fast removal of the tissue from the bladder. With regard to the resection weight, more prostate adenoma tissue was removed in the B-TUERP-M group can than the B-TUERP group (65.73 VS 60.73 gm, p-value 0.027). In the B-TUERP group the adenoma attaches to the bladder neck, which may be a cause of retention of some adenoma. It was also found in this study that the post-operative hematocrit was lower in the B-TUERP group than in the B-TUERP-M group (33.18% vs 35.16%, p-value 0.007). However, the blood transfusion requirements were no different between the two groups (17.0% vs 7.7%, p-value 0.096). Regarding the post-operative results, better outcomes were achieved in the B-TUERP-M, specifically Qmax, PVR and PSA at 1, 3 and 6 month, which corresponds to the more effective resection weight removed in the B-TUERP-M group than the B-TUERP group. Chawat et al reported that the amount of resected prostate tissue from transurethral prostatectomy was related to outcome and concluded that the amount of resected prostate tissue had a slight influence on the difference in LUTS and QoL after TURP.[15] In this study, only IPSS at 6 months that the B-TUERP-M group is lower than the B-TUERP group. There was no difference between the two groups in post-operative QOL at 1, 3 and 6 months.

The main limitation of this study was the relatively short follow-up time and further studies with longer follow-up and randomized control trials are warranted to assess and compare the durability and the results of these two techniques.

Conclusion

Use of a morcellator in TUERP for surgical treatment of benign prostatic hyperplasia can achieve a better outcome with regard to operative time, resection weight of prostatic adenoma, post-operative urine flow rate, post-void residual urine volume, PSA and International Prostate Symptom Score than TUERP without morcellation.

References

1. Reich O, Gratzke C, Stief CG. Techniques and long-term results of surgical procedures for BPH. Eur Urol 2006;49:970-8.
2. Jacobsen SJ, Girman CJ, Lieber MM. Natural history of benign prostatic hyperplasia. Urology 2001;58:5-16.
3. Mebust WK, Holtgrewe HL, Cockett AT, Peters PC. Transurethral prostatectomy: immediate and postoperative complications. A cooperative study of 13 participating institutions evaluating 3,885 patients. J Urol 1989;141:243-7.
4. Borboroglu PG, Kane CJ, Ward JF, Roberts JL, Sands JP. Immediate and postoperative complications of transurethral prostatectomy in the 1990s. J Urol 1999;162:1307-10.
5. Chandrasekar P, Kapasi F, Virdi J. A prospective randomized study between transurethral vaporization using plasmakinetic energy and transurethral resection of the prostate. Eur Urol Suppl 2006;5:309.
6. Eaton AC, Francis RN. The provision of transurethral prostatectomy on a day-case basis using bipolar plasmakinetic technology. BJU Int 2002;89:534-7.
7. Mohamed S, Ahmed T, Mahmoud M, Elawady H, Abuelnaga M, Shabayek M, et al. Two-year follow-up in bipolar transurethral enucleation and resection of the prostate in comparison with bipolar transurethral resection of the prostate in treatment of large prostate. Randomized controlled trial. J Urol 2019;133:192-8.
8. Liu C, Zheng S, Li H, Xu K. Transurethral enucleation and resection of prostate in patients with benign prostatic hyperplasia by plasmakinetic. J Urol 2010;184:2440-5.
9. Thaidumrong T, Duangkae S, Jiramanee V, Kalapong J, Psansalhidikam P, Tuipae K. Transurethral anatomical enucreation of prostate (TUAEP) in benign prostatic hyperplasia with bipolar system: first study in Thailand. J Med Assoc Thai 2019;102:20-5.
10. Emberton M, Andriole GL, de la Rosette J, Djavan B, Hoefner K, Navarrete RV, et al. Benign prostatic hyperplasia: a progressive disease of aging men. Urology 2003;61:267-73.
11. Zhao Z, Zeng G, Zhong W, Mai Z, Zeng S, Tao X. A prospective randomized trial comparing plasmakinetic enucleation to standard transurethral resection of the prostate for symptomatic benign prostate hyperplasia three-year follow-up results. Eur Urol 2010;58:752-8.
12. Neill MG, Gilling PJ, Kennett KM, Framton CM, Westenberg AM, Fraundorfer MR, et al. Randomized trial comparing holmium laser enucleation of prostate with plasmakinetic enucleation of prostate for treatment of benign prostatic hyperplasia. Urology 2006;68:1020-4.
13. Davide A, Celeste M, Alessandro V, Herrmnn TRW, Lima E, Mirone V, et al. Bipolar endoscopic enucleation versus bipolar transurethral resection of the prostate: an ESUT systematic review and cumulative analysis. World J Urol 2020;38:1177-86.
14. Julia F, Rodrigo S, Philipp P, Single A, Lusuardi L, Netsch C, et al. Morcellator after endoscopic enucleation of the prostate: efficiency and safety of currently available devices. Eur Urol 2022;8:532-44.
15. Angsurak C, Kochakarn W, Leenanupunth C, Kongchareonsombat W, Viseshsindh W, Kijvikai K, et al. Is the amount of resected prostate tissue from transurethral prostatectomy related to outcome?. Thai J Urol 2018;39:9-16.

Original Article

Intravesical recurrence in upper tract urothelial carcinoma patients after radical nephroureterectomy in Rajavithi Hospital

Niti Chamchoy, Chawawat Gosrisirikul

Division of Urology, Department of Surgery, Rajavithi Hospital, Bangkok, Thailand

Keywords:
Upper tract urothelial carcinoma, intravesical recurrence, nephroureterectomy, predictive factors

Abstract

Objective: Upper tract urothelial carcinoma (UTUC) is a malignant disease which is challenging to manage. The modalities for diagnosis and accurate clinical staging are limited, radical nephroureterectomy (RNU) with bladder cuff excision being the gold standard for treatment of UTUC. Subsequent intravesical recurrence (IVR) following RNU is a common problem. This study investigated the risk factors that affect IVR in Rajavithi Hospital. The objective of this study is to investigate whether the risk factors affect intravesical recurrence in UTUC patients after RNU.

Materials and Methods: This retrospective study evaluated 94 patients who had undergone RNU in Rajavithi Hospital for UTUC between November 2006 and February 2021; 69 patients were included in the analysis. Data was analyzed to investigate risk factors that impact IVR and IVR-free survival using Kaplan-Meier and Cox proportional regression methods.

Results: Out of 69 patients, at a mean follow up of 24 months, IVR occurred in 27 patients (39.1%). The overall postoperative 5-year IVR-free survival was 51.3%. Multivariate analysis indicated significant risk factors were high- grade tumor (adjusted HR = 3.47, 95%CI: 1.12-10.76, p = 0.031), ureterorenoscopy (URS) (adjusted HR = 3.45, 95%CI: 1.35-8.81, p = 0.01) and tumor multifocality (adjusted HR = 2.75, 95%CI: 1.02-7.38, p = 0.045). Postoperative 5-year IVR-free survival was significantly different for high-grade tumor compared with low-grade tumor (36.6% vs 82%, p = 0.006) and multiple tumors compared with a solitary tumor (18.4% vs 68.8%, p = 0.003) but there was no significant difference in URS compared with no URS (46.3% VS 51.6, p = 0.158).

Conclusion: The risk factors that affect intravesical recurrence in UTUC patients after Radical nephroureterectomy are high-grade tumor, tumor multifocality, and URS.

Insight Urol 2023;44(1):14-20. doi: doi: 10.52786/isu.a.67

Corresponding author: Niti Chamchoy

Address: Division of Urology, Department of Surgery, Rajavithi Hospital, 2 Phayathai Road, Ratchathewi District, Bangkok 10400, Thailand

E-mail: mathdavil@gmail.com

Manuscript received: April 9, 2023

Revision received: May 8, 2023

Accepted after revision: May 28, 2023

Introduction

Upper tract urothelial carcinoma (UTUC) is a malignant disease, accounting for approximately 5-10% of urothelial neoplasms and 10% of renal tumors.[1] Radical nephroureterectomy (RNU) with bladder cuff excision is the standard treatment for localized UTUC.[2] In comparison with bladder carcinoma, the prognosis of UTUC is relatively poor even though there are various treatment modalities. However, intravesical recurrence (IVR) after RNU is a common problem in patients with UTUC, this event can occur in 27% to 49% of patients, and the prognostic impact of IVR on oncologic outcomes remains unclear.[3,4] Previous studies have reported that environmental and clinicopathological factors, such as gender, tumor multifocality, pT stage and surgical approach, and diagnostic ureteroscopy could affect IVR after RNU.[1,5-8] Due to the relatively high occurrence rate of IVR, European Association of Urology (EAU) guidelines recommend that follow-up cystoscopy should be performed to detect IVR in patients who undergo RNU.[9] For this reason, identifying the risk factors that predict IVR of UTUC after RNU is essential to minimize the need for invasive examinations and facilitate the selection of patients who may benefit from early surgical intervention. Future studies should be performed to find a novel way to reduce the potential risk of IVR after RNU, for example the use of chemoprophylaxis.

Some clinicopathologic prognostic factors of IVR have been validated, but no consensus has been reached for variables that will consistently predict which patients will develop IVR.[10-12] The aim of this study is to identify the prognostic impact of IVR on oncologic outcomes and to identify the clinicopathologic factors that predict IVR in patients treated with RNU for UTUC.

This study was carried out at Rajavithi Hospital with the aim of investigating the risk factors that affect IVR.

Materials and Methods

Patients and inclusion criteria

Ninety-four patients underwent RNU with bladder cuff resection in Rajavithi Hospital between November 2006 and February 2021. All patients underwent routine preoperative cystoscopy before RNU to identify the possibility of synchronous bladder cancer.

Exclusion criteria

Out of the 94 patients, 25 were excluded as a result of synchronous bladder cancer, prior history of bladder cancer, status post cystectomy, no pathologic diagnosis for urothelial carcinoma or positive margin, or incomplete data (Figure 1).

Methods

A total of 69 patients were included in the study cohort. Clinical data on demographic characteristics and follow-up medical records were retrospectively collected after obtaining ethical board review approval from Rajavithi Hospital (study number: 64209).

All patients underwent standard open or laparoscopic RNU with bladder cuff resection, performed using the extravesical technique, where the ureter was dissected through the detrusor hiatus for complete resection of the intraluminal portion of the ureter. The bladder cuff was completely removed, and the bladder was closed using a continuous absorbable suture.

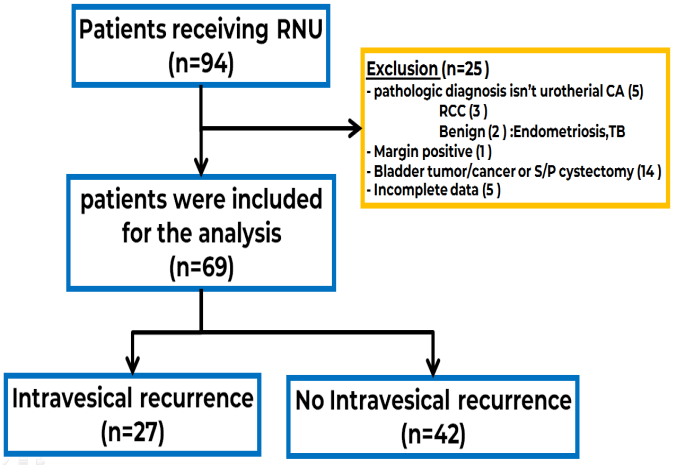


Figure 1. Flow chart of the study

Early ligation of the distal ureter was not routinely performed, and lymphadenectomy was not performed, with the exception of patients with suspiciously enlarged lymph nodes.

None of the 69 patients underwent neoadjuvant chemotherapy.

Diagnostic ureterorenoscopy (URS) was performed before RNU, but only for patients with equivocal diagnostic cases. Patients in whom preoperative URS was not deemed necessary had relatively definite tumor lesions on the radiologic image.

Pathologic evaluation

Tumors were staged according to the Tumor Node Metastasis classification and graded in accordance with the 2004 World Health Organization classification. Tumor location was defined as the renal pelvis, ureter, or both. Tumor multifocality was defined as pathologic confirmation of the synchronous presence of tumors in any location in the renal pelvis and ureter. Concomitant carcinoma in situ (CIS) was defined as the presence of CIS at any location in the renal pelvis and ureter.

Follow-up

All patients underwent cystoscopy every three months for the first two years, every six months for the next two years, and annually after that to check for the recurrence or occurrence of bladder tumors

Abdomen and chest CT and bone scans were performed when clinically indicated. IVR was defined as pathologic confirmation of bladder cancer through cystoscopic biopsy or transurethral resection. IVR excluded any tumor relapse outside the bladder.

Statistical analyses

The clinicopathologic factors affecting IVR were compared using the Chi-square test and Fisher exact test for categorical data and the Student t-test for continuous variables.

The probability of intravesical recurrence-free survival was estimated using the Kaplan-Meier method, and log-rank test values were used to assess the level of statistical difference.

The prognostic effects of clinicopathologic variables on IVR were estimated using univariate and multivariate Cox proportional hazards regression models.

Hazard ratios (HRs) with 95% confidence intervals (CIs) were used to assess the strength of the individual variables. Statistical analysis was performed with Stata v.17, and statistical significance was defined as a $p < 0.05$.

Results

The median follow-up for the whole cohort was 24 months (interquartile range, 3-120 months). 27 (39.1%) patients experienced IVR within 6.4 months (interquartile range, 1.5-12.5 months) of the median interval between RNU and the first IVR.

Table 1 shows patient characteristics. The average age of patients was 65 years, 40 (58%) were male, 53 (76.8%) had underlying diseases, and 36 (52.2%) were smokers. Tumor classification factors were as follows: high T stage 35 (52.2%), N0 60 (87%), M0 67 (97.1%) and high-grade tumor 50 (72.5%). The locations of the primary tumor were 40 (58%) on the right side and 40 (58%) on the renal pelvis. The tumor was almost restricted to a solitary mass 50 (72.5%) and no CIS 60 (87%). Patients who underwent URS numbered[21] (30.4%), and the most frequent surgical method for RNU was the open technique 56 (81.2%).

Univariate Cox analysis showed that only M1 stage (HR, 11.67;95% CI, 1.28-106.2; p = 0.029), high grade tumor (HR, 4.04;95% CI, 1.38-11.84; p = 0.011), tumor multifocality HR, 3.06;95% CI, 1.43-6.55; p = .0.004) increase the probability of IVR (Table 2).

Then, we continued the analysis with multivariate Cox analysis to eliminate confounding factors and the outcome also showed that high grade tumor (HRadj, 3.47;95% CI, 1.12-10.76; p = 0.031), URS (HRadj, 3.45;95% CI, 1.35-8.81; p = 0.010), and tumor multifocality (HRadj, 2.75;95% CI, 1.02-7.38; p = 0.045) were independent significant factors for poor prognosis for IVR (Table 2).

In the multivariate analysis table, we only show factors that were found to be significant in both the multivariate and the univariate analysis, as these factors were further analyzed in the multivariate analysis.

The overall 5-year intravesical recurrent survival was 51.3%. The 5-year intravesical recurrent survival was 36.6% for high-grade tumors compared with 82% for low-grade tumors (p = 0.006), and 18.4% for multiple tumors compared with

Table 1. Patient characteristics

Characteristics	Total (n = 69)	
ECOG		(%)
0	24	(34.8)
1	35	(50.7)
2	10	(14.5)
Urine cytology		
No	51	(73.9)
Yes	18	(26.1)
Result of Urine cytology, (n = 18)		
No cancer	11	(61.1)
Cancer	7	(38.9)
URS	21	(30.4)
Location of Tumor		
Side		
Right	40	(58.0)
Left	29	(42.0)
Location of Primary Tumor		
Renal pelvis	40	(58.0)
Ureter proximal	13	(18.8)
Ureter distal	16	(23.2)
Multifocal		
Solitary	50	(72.5)
Multiple	19	(27.5)
CIS		
No	60	(87.0)
Yes	9	(13.0)
Surgical Method		
Open	56	(81.2)
Laparoscopic	13	(18.8)

Characteristics	Total (n = 69)	
		(%)
No. of patients	69	(100.0)
Age (years)	65.62 ± 13.15	
Sex		
Female	29	(42.0)
Male	40	(58.0)
Underlying diseases	53	(76.8)
Diabetes mellitus	20	(29.0)
Hypertension	40	(58.0)
Chronic kidney disease	14	(20.3)
Other	9	(13.0)
Smoking	36	(52.2)
T Stage		
T1	7	(10.1)
T2	27	(39.1)
≥T3	35	(50.7)
N Stage		
0	60	(87.0)
1	5	(7.2)
2	4	(5.8)
M Stage		
0	67	(97.1)
1	2	(2.9)
Grade		
Low	19	(27.5)
High	50	(72.5)

CIS = carcinoma in situ, URS = ureterorenoscopy, ECOG = Eastern Cooperative Oncology Group

68.8% for solitary tumors (p = 0.003). However, patients who underwent URS (compared with no URS) did not show statistically significant differences in 5-year intravesical recurrent survival (46.3% VS 51.6, p = 0.158) (Figure 2).

Discussion

This study found that 39.1% of patients with UTUC experienced IVR within a median interval of 6.4 months between RNU and the first IVR, which is in agreement with previous studies (27-49%).[3,4] However, the occurrence of IVR following RNU did not affect CSS and OS when IVR was detected early and the decision for surgical intervention was made based on scheduled cystoscopic follow-up.[13] Currently; two major hypotheses explain the pathogenesis of IVR after RNU for UTUC:[14,15]

1. Pan urothelial field-effect theory: preoperative carcinogen exposure in the entire urothelium accounts for independent tumor development following RNU

2. Intraluminal seeding and implantation of a single transformed cell theory: the bladder is continuously exposed to cancer cells dropping from the upper urinary tract before and during RNU.

The risk factors described in the previous studies are age, gender, tumor multiplicity, TNM stage, grade, tumor location, hydronephrosis, tumor size, previous/concomitant bladder tumors, carcinoma in situ, surgical mode, distal ureter management and URS before RNU.[13,16-24] Among these factors, a history of a prior bladder tumor is the most frequently reported, we excluded the patients with previous/concomitant bladder cancer because the incidence of IVR in those patients is related to localized disease instead of UTUC.

However, our study found that presence of a high grade tumor, tumor multifocality, and URS were independent risk factors for increased probability of IVR. We grouped large tumor size and hydronephrosis as the high stage group. In terms of 5-year intravesical recurrence-free survival, only high-grade tumors and multiple tumors showed a decrease, but URS did not. We chose to perform URS procedures only in patients with equivocal diagnostic cases from imaging, not for all patients. Patients who did not receive preoperative URS had relatively definite tumor lesions on the radiologic image, which could have affected the results, although the pathologic outcomes were not significantly different. Therefore, the lack of significance in 5-year recurrence free survival between the two groups in the study

Table 2. Univariate and multivariate Cox regression analyses predicting intravesical recurrence

Factors	Univariate analysis			Multivariate analysis		
	HR	95%CI	P-value	HRadj	95%CI	P-value
Age ≥ 65 years old	1.53	(0.67-3.50)	0.317			
Male sex	1.25	(0.58-2.71)	0.572			
Underlying diseases	1.79	(0.67-4.76)	0.246			
Smoker	1.83	(0.81-4.13)	0.144			
T stage						
T1	1.00	Reference				
T2	1.65	(0.45-5.99)	0.446			
≥ T3	1.38	(0.37-5.13)	0.628			
N stage						
0	1.00	Reference				
1	2.30	(0.28-18.6)	0.436			
2	0.65	(0.08-5.02)	0.680			
M stage						
0	1.00	Reference		1.00	Reference	
1	11.67	(1.28-106.2)	0.029	3.67	(0.36-36.98)	0.269
Tumor grade						
Low	1.00	Reference		1.00	Reference	
High	4.04	(1.38-11.84)	0.011	3.47	(1.12-10.76)	0.031
ECOG						
0-1 (low)	1.00	Reference				
2-3 (high)	2.10	(0.84-5.24)	0.113			
Urine cytology	1.83	(0.80-4.17)	0.152			
Result of urine cytology, (n = 18)						
No cancer	1.00	Reference				
Cancer	0.52	(0.13-2.11)	0.362			
URS	1.72	(0.80-3.70)	0.163	3.15	(1.35-8.81)	0.010
Result of ureteroscopy, (n = 17)						
No cancer	1.00	Reference				
Cancer	0.04	(0.01-0.25)	0.001			
Left side	1.08	(0.49-2.39)	0.841			
Location of primary tumor						
Renal pelvis	1.00	Reference				
Ureter	1.25	(0.59-2.67)	0.562			
Tumor multifocality	3.06	(1.43-6.55)	0.004	2.75	(1.02-7.38)	0.045
CIS present	2.98	(1.32-6.72)	0.009	2.08	(0.75-5.78)	0.161
Surgical Method						
Open	1.00	Reference				
Laparoscopic	2.23	(0.96-5.20)	0.062			
Duration from URS to RNU > 1 month	2.19	(0.58-8.21)	0.245			

may be attributed to the fact that the URS group exhibited a comparatively lower TNM stage than the non-URS group.

High grade tumor and tumor multifocality are non-modifiable factors. The inclusion of the URS procedure is the only modifiable factor that doctors need to decide upon, whether to do it or not, based on the benefit for diagnosis and risk of IVR, specifically the potential for intraluminal seeding as a consequence of ureteroscope manipulation and irrigation, retrograde flow, increased urine flow rate and intraluminal pressure which may lead to the shedding of tumor cells.[25]

Current evidence suggests that adjuvant intravesical chemotherapy after RNU decreased IVR risk.[26-28] The agents used are mitomycin-c, gemcitabine, or pirarubicin.[29] However, our study does not analyze the effect of adjuvant intravesical chemotherapy on IVR because of the small sample size and incomplete data.

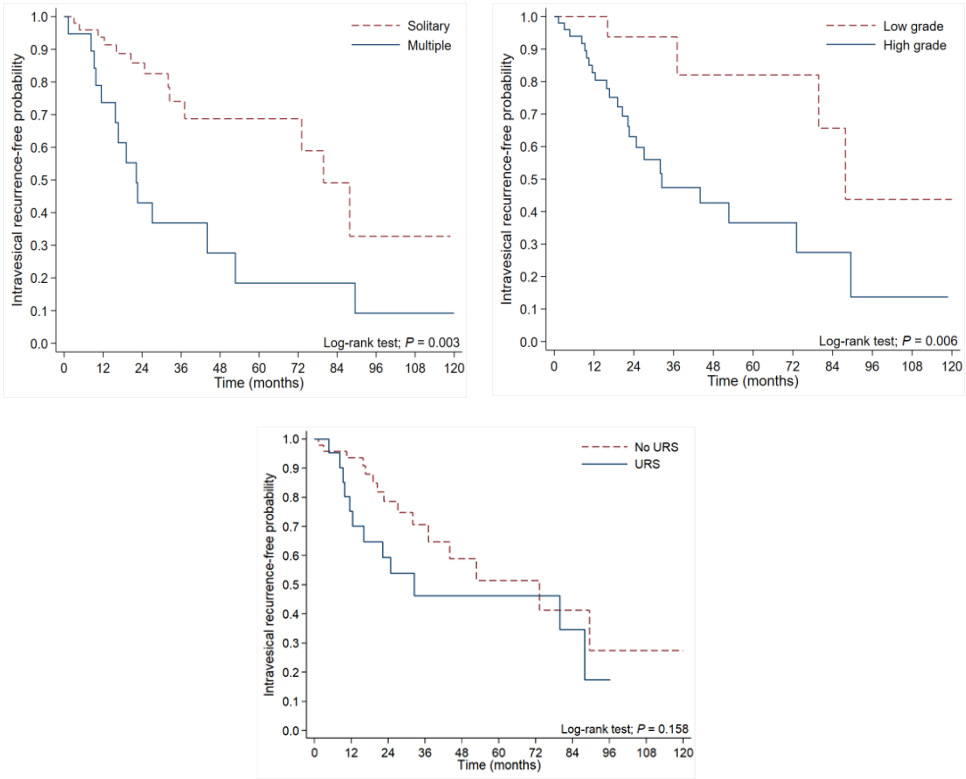


Figure 2. Kaplan-Meier Curves of the 5-year Intravesical Recurrence-free Period Stratified by Tumor Grade, Tumor Multifocality, and URS

The limitations of this study are its retrospective design, small patient population, and a relatively short period of follow-up (median follow-up = 2 years).

Other limitations could be the presence of microscopic, concurrent bladder cancer. Although we excluded patients with a previous history of bladder cancer, there could be some portion of cancer cells in the bladder of some patients.

Conclusions

Our results suggest that the factors that increase IVR risk in UTUC patients after radical nephroureterectomy are high-grade tumor, tumor multifocality, and URS. To reduce IVR, risk-based follow-up and preventive methods should be considered for patients with these risk factors.

Conflict of Interest

The authors declare no conflicts of interest.

References

1. Tan P, Xie N, Yang L, Liu L, Tang Z, Wei Q. Diagnostic ureteroscopy prior to radical nephroureterectomy for upper tract urothelial carcinoma increased the risk of intravesical recurrence. Urol Int 2017;100:92-9.
2. Margulis V, Shariat S, Matin S, Kamat A, Zigeuner R, Kikuchi E, et al. Outcomes of radical nephroureterectomy: A series from the upper tract urothelial carcinoma collaboration. Cancer 2009;115:1224-33.
3. Zigeuner R, Hutterer G, Chromecki T, Rehak P, Langner C. Bladder tumour development after urothelial carcinoma of the upper urinary tract is related to primary tumour location. BJU Int 2006; 98:1181-6.
4. Xylinas E, Rink M, Cha E, Clozel T, Lee R, Fajkovic H, et al. Impact of distal ureter management on oncologic outcomes following radical nephroureterectomy for upper tract urothelial carcinoma. Eur Urol 2014;65:210-7.
5. Novara G, De Marco V, Dalpiaz O, Gottardo F, Bouygues V, Galfano A, et al. Independent predictors of metachronous bladder transitional cell carcinoma (TCC) after nephroureterectomy for TCC of the upper urinary tract. BJU Int 2008;101:1368-74.
6. Xylinas E, Colin P, Audenet F, Phe V, Cormier L, Cussenot O, et al. Intravesical recurrence after radical nephroureterectomy for upper tract urothelial carcinomas: predictors and impact on subsequent oncological outcomes from a national multicenter study. World J Urol 2013;31:61-8.
7. Seisen T, Granger B, Colin P, Léon P, Utard G, Renard-Penna R, et al. A systematic review and meta-analysis of clinicopathologic factors linked to intravesical recurrence after radical nephroureter-

ectomy to treat upper tract urothelial carcinoma. Eur Urol 2015; 67:1122-33.
8. Rouprêt M, Babjuk M, Compérat E, Zigeuner R, Sylvester RJ, Burger M, et al. European association of urology guidelines on upper urinary tract urothelial cell carcinoma: 2015 update. Eur Urol 2015;68:868-79.
9. Rouprêt M, Babjuk M, Burger M, Capoun O, Cohen D, Compérat E, et al. European association of urology guidelines on upper urinary tract urothelial carcinoma: 2020 update. Eur Urol 2021;79:62-79.
10. Xylinas E, Kluth L, Passoni N, Trinh QD, Rieken M, Lee RK, et al. Prediction of intravesical recurrence after radical nephroureterectomy: development of a clinical decision-making tool. Eur Urol 2014;65:650-8.
11. Ishioka J, Saito K, Kijima T, Nakanishi Y, Yshida S, Yokoyama M, et al. Risk stratification for bladder recurrence of upper urinary tract urothelial carcinoma after radical nephroureterectomy. BJU Int 2015;115:705-12.
12. Fradet V, Mauermann J, Kassouf W, Rendon R, Jacobsen N, Fairey A, et al. Risk factors for bladder cancer recurrence after nephroureterectomy for upper tract urothelial tumors: results from the canadian upper tract collaboration. Urol Oncol 2014;32:839-45.
13. Lee CH, Ku JY, Jeong CW, Ku JH, Kwak C, Kim HH, et al. Predictors for intravesical recurrence following radical nephroureterectomy for upper tract urothelial carcinoma: a national multicenter analysis. Clin Genitourin Cancer 2017;15:e1055-61.
14. Habuchi T, Takahashi R, Yamada H, Kakehi Y, Sugiyma T, Yocshida O. Metachronous multifocal development of urothelial cancers by intraluminal seeding. Lancet 1993;342:1087-8.
15. Jones T, Wang M, Eble J, MacLennan G, Lopez-Beltran A, Zhang S, et al. Molecular evidence supporting field effect in urothelial carcinogenesis. Clin Cancer Res 2005;11:6512-9.
16. Fang D, Xiong GY, Li XS, Chen XP, Zhang L, Yao L, et al. Pattern and risk factors of intravesical recurrence after nephroureterectomy for upper tract urothelial carcinoma: a large Chinese center experience. J Formos Med Assoc 2014;113:820-7.
17. Matsui Y, Utsunomiya N, Ichioka K, Ueda N, Yoshimura K, Terai A, et al. Risk factors for subsequent development of bladder cancer after primary transitional cell carcinoma of the upper urinary tract. Urology 2005;65:279-83.
18. Favaretto RL, Shariat SF, Chade DC, Godoy G, Adamy A, Kaag M, et al. Effect of tumor location on prognosis in patients treated with radical nephroureterectomy at Memorial Sloan- Kettering Cancer Center. Eur Urol 2010;58:574-80.
19. Lughezzani G, Sun M, Perrotte P, Shariat SF, Jeldres C, Budus L, et al. Gender-related differences in patients with stage I to III upper tract urothelial carcinoma: results from the Surveillance, Epidemiology, and End Results database. Urology 2010;75:321-7.
20. Xylinas E, Rink M, Cha EK, Clozel T, Lee RK, Fajkovic H, et al. Impact of distal ureter management on oncologic outcomes following radical nephroureterectomy for upper tract urothelial carcinoma. Eur Urol 2014;65:210-7.
21. Shariat SF, Godoy G, Lotan Y, Droller M, Karakiewicz PI, Raman JD, et al. Advanced patient age is associated with inferior cancer-specific survival after radical nephroureterectomy. BJU Int 2010;105:1672-7.
22. Novara G, Matsumoto K, Kassouf W, Walton TJ, Fritsche HM, Bastian PJ, et al. Prognostic role of lymphovascular invasion in patients with urothelial carcinoma of the upper urinary tract: an international validation study. Eur Urol 2010;57:1064-71.
23. Yuan H, Chen X, Liu L, Yang L, Pu C, Li J, et al. Risk factors for intravesical recurrence after radical nephroureterectomy for upper tract urothelial carcinoma: a meta analysis. Urol Oncol 2014;32:989-1002.
24. Chen XP, Xiong GY, Li XS, Matin SF, Garcia M, Fang D, et al. Predictive factors for worse pathological outcomes of upper tract urothelial carcinoma: experience from a nationwide high-volume centre in China. BJU Int 2013;112:917-24.
25. Liu P, Su XH, Xiong GY, Li XS, Zhou LQ. Diagnostic ureteroscopy for upper tract urothelial carcinoma is independently associated with intravesical recurrence after radical nephroureterectomy. Int Braz J Urol 2016;42:1129-35.
26. Wu WJ, Ke HL, Yang YH, Li CC, Chou YH, Huang CH. Should patients with primary upper urinary tract cancer receive prophylactic intravesical chemotherapy after nephroureterectomy? J Urol 2010;183:56-61.
27. O'Brien T, Ray E, Singh R, Coker B, Beard R, British association of urological surgeons section of oncology. Prevention of bladder tumours after nephroureterectomy for primary upper urinary tract urothelial carcinoma: a prospective,multicentre, randomised clinical trial of a single postoperative intravesical dose of mitomycin C (the ODMIT-C Trial). Eur Urol 2011;60:703-10.
28. Ito A, Shintaku I, Satoh M, Ioritani N, Aizawa M, Tochigi T, et al. Prospective randomized phase II trial of a single early intravesical instillation of pirarubicin (THP) in the prevention of bladder recurrence after nephroureterectomy for upper urinary tract urothelial carcinoma: the THP monotherapy study group trial. J Clin Oncol 2013;31:1422-7.
29. Zabell J, Konety BR. Management strategies for non-muscle-invasive bladder cancer (Ta, T1, and CIS). In: Partin AW, Dmochowski RR, Kavoussi LR, Peters CA, editors. Campbell-Walsh-Wein Urology. 12th ed. Pennsylvania: Elsevier; 2020. p. 3091-111.

Original Article

Five-year overview of penile prosthesis implantation: general considerations from real-life practice

Dechapol Buranapitaksanti[1,5,6,7,8], Arnantkorn Chauvanasmith[2], Ussapol Tantarawongsa[3], Akanae Wongsawat[4]

[1]Navavej International Hospital, [2]Yanhee Hospital, [3]Police General Hospital, [4]Medpark Hospital, [5]Churarat 3 International Hospital, [6]Ladprao Hospital, [7]Piyavate Hospital, [8]Kasemrad Ramkamhaeng Hospital, Bangkok, Thailand

Keywords:
Penile prosthesis implantation, general consideration, real-life practice

Abstract

Objective: Penile prosthesis (PP) is the third-line therapy for erectile dysfunction in patients who do not respond to pharmacotherapy or who prefer a permanent solution to their problem. Even though the satisfaction rate is high, implantation is irreversible, and complications such as infection can lead to catastrophic outcomes. The objective of this study is to provide a 5-year (2018-2022) overview of patients who underwent penile prosthesis implantation, including techniques using both an inflatable penile prosthesis and semirigid prosthesis.

Materials and Methods: Aspects of the study include pre-surgical counseling, patient and device selection, operative technique, and special considerations in relation to implantation in complex cases, such as those involving corporal fibrosis, Peyronie's disease, or revision procedures.

Results: This 5-year overview demonstrates that the techniques remain effective and safe (0% infection rate) with a high satisfaction rate (84%) when compared to several prior studies. Better understanding and advancement in surgical techniques provide good outcomes; thus, implantation of a penile prosthesis is a good option for treatment of erectile dysfunction.

Conclusion: This 5-year review of PP implantation carried out in 35 patients by a single surgeon shows a very low complication rate after surgery with a high level of patient satisfaction. To maximize the potential for a good outcome, prior to surgery the physical status of patients should be evaluated and counseling is essential. In patients identified as being at a high risk, the implantation team should be prepared for complications using evidence-based data.

Insight Urol 2023;44(1):21-7. doi: 10.52786/isu.a.68

Corresponding author: Dechapol Buranapitaksanti
Address: Navavej International Hospital, Bangkok, Thailand
E-mail: buranadecha@gmail.com
Manuscript received: January 21, 2023
Revision received: May 16, 2023
Accepted after revision: June 2, 2023

Introduction

In 1973, Dr. F. Brantley Scott introduced the first Inflatable Penile Prosthesis (IPP).[1] Just a year later, in 1974, Dr. Michael Small and Dr. Hernan Carrion introduced their competitor device, a precursor to semirigid malleable devices. Since that date practices related to the PP have been developed with the use of materials and surgical techniques that have increased rigidity, durability, and patient satisfaction while decreasing postoperative complications. The introduction of Phosphodiesterase-5 inhibitors (PDE5-inh.) in 1998 changed the approach to treatment of erectile dysfunction. However, the American Urological Association (AUA) Guidelines showed that implantation of a penile prosthesis remained a promising solution for patients with erectile dysfunction (ED) in whom conventional medical therapies had failed.[2]

The objective of this article is to report on a 5-year overview of PP implantation that was either carried out or supervised by a single surgeon (DB) across many centers in Thailand. The article focuses on pre-operative considerations (patient selection, preparation, and counseling), intra-operative evidence-based decision-making in complex cases (such as Peyronie's disease, corporal fibrosis, and revision), and post-operative outcomes (complications and patient satisfaction).

Materials and Methods

This retrospective study included 35 ED patients who underwent implantation of a penile prosthesis, with ether an IPP and Semirigid malleable penile prosthesis from 2018 to 2022. The procedures took place across many centers, and were either performed or supervised by a single surgeon.

Patient selection

All patients were counseled, operated upon and followed up by implantation specialists (DB, AC, UT, AW). Data about sexual function, degree of ED, previous medical and surgical ED treatment, physical examination and current medical diseases was collected and analyzed for all patients. ED was defined as the inability to achieve and maintain an erection sufficient for satisfactory sexual performance.[3] If a patient had Peyronie's disease the degree of curvature and erectile function had been measured carefully prior to implantation. Revision surgery was carried out in cases of corporal fibrosis, which had occurred as a result of infected implantation or Priapism. The potential for a high complication rate (infection, erosion, deformity, perforation or urethral injury) needed to be discussed before proceeding.

16% of implanted patients were seeking revision for reasons outside of mechanical dysfunction or erosion.[4] This dissatisfaction was due to desire for "perfect" surgery. The identification of these patients is necessary to achieve the desired post-operative outcome and satisfaction. Pre operative counseling is a primary tool to identify the perception of the patients' expectation. IPP mainly restores physiological function (girth, sensation, ejaculation) but unrealistic expectations (increasing penile length and circumference) are at risk of post-operative dissatisfaction.[5]

Pre-operative preparation included medical clearance for patients with cardiovascular, endocrine, or other diseases. A diagnosis of ED is often a marker of underlying coronary artery disease.[6] This population was at high risk of cardiovascular events and needed to be carefully assessed. Patients with diabetes and a hemoglobin A1C greater than 8.5% have been shown to experience increased postoperative surgical site infections in association with PP.[7] Antiplatelet or anticoagulant therapy should be discontinued prior to the operation, or the operation postponed if patients were at high risk under EAU/AUA guidelines for patient selection.[8]

Device selection

The decision regarding device selection was made in consultation with the patient and surgeon, taking into account various factors such as the etiology of ED, penile length and anatomy, prior surgery, manual dexterity, spinal cord injuries, and prior device explant. All of these factors influenced the device recommendation. For instance, patients with limited manual dexterity and difficulty with device inflation/deflation were more suited to a semirigid implant. Patients with corporal fibrosis that limited the space in the corporal bodies were better suited to a narrow cylinder or a lower-diameter semi-rigid implant. In addition, the surgeon's preference and experience, device availability, and cost could also impact device selection.

Preoperative antibiotics prophylaxis

The most recent update from the American Urological Association guidelines advocates the use of an aminoglycoside plus cephalosporin or vancomycin as first-line prophylaxis.[9] Vancomycin 1 g plus Ceftriazone 2 g was administrated intravenously to all patients if no allergic history. Patients showered with Chlorhexidine solution on the day of surgery.

Technique

The technique for penile prosthesis implantation involves several steps. Firstly, the patient is prepared for surgery, and anesthesia is administered. The skin is then prepped, and a urethral catheter is inserted. The penis and scrotum are exposed using an Ioban® drape.

A penoscrotal incision is made, followed by corporotomies. Blunt tip scissors may be used to dilate the corporal bodies, and sequential Brooks' dilators are used to dilate down to the crus proximally and distally to the mid glans. The implant selected depends on the patient's anatomy and etiology of ED. In the case of IPP, an ectopic reservoir is placed via the external inguinal ring anterior to the transversalis fascia. The scrotal pump is placed by developing a subdartos plane.

Once all components are connected and in position, the skin is closed in two layers, and no drain is used. The operative time and blood loss are recorded, and the patient stays in the hospital for one night. The Foley catheter is removed before discharge, and antibiotics are switched to Amoxiklav 1 g twice daily for 2 weeks. Patients are instructed to avoid showering for a week, and at the one-week appointment, they are interviewed about postoperative pain, fever, urination, sensation, general appearance, and any other concerns. Sexual intercourse can start at 6 weeks after the operation. The satisfaction rate is assessed by a telephone interview after 6 weeks.

Results

Baseline characteristics

A total of 35 patients underwent penile prosthesis implantation between 2018-2022. 28 cases were implanted with semirigid implant Coloplast Genesis (Coloplast corp., Minneapolis, MN, USA) and 7 cases with IPP Coloplast Titan (Coloplast corp. Minneapolis, MN, USA).

The mean age was 59.5 (29-85) years. Causes of ED were vasculogenic (cardiovascular, diabetes) 27 (77.1%), neurogenic (spinal cord injury) 1 (2.8%), anatomical and structural disease (priapism and corporal fibrosis) 4 (11.4%), hypogonadism (post orchiectomy) 1 (2.8%) and Peyronie's disease 2 (5.7%).

Four patients had been undergoing revision surgery. Mean duration to initial malfunction was 2 (1-3) years. Two patients underwent revision with new IPP due to system malfunction (implanted by other centers), 1 patient underwent revision from a semi-rigid implant to IPP and 1 patient had revision from a semi-rigid implant to appropriate size and length. Four cases had corporal fibrosis (3 from untreated Priapism and 1 from infected prior implantation procedure) and 2 cases had Peyronie's disease (one with ED and one without ED). All ED patients were classified as severe ED, determined using the IIEF score (5-7) and were Phosphodiesterase-5 inhibitors (PDE-5inh.) non-responders, had contra-indications for PDE-5 inh. or could not tolerate side effects from PDE-5 inh. (Table 1).

Intra-operative events

Overall, the mean operative time was 77 minutes (ranging from 45 to 210 minutes) and the mean blood loss was 65 ml (ranging from 50 to 200 ml). A prolonged operative time of 3.5 hours and excess blood loss of 200 ml were observed in a patient with severe corporal fibrosis. During corporal dilatation in a patient with Peyronie's disease, one case of urethral injury was recorded. In this case a penoscrotal incision and corporotomy were extended to expose the perforated site, and a small perforation at the distal urethra was repaired with double layers of absorbable suture. Vigorous irrigation with NSS and Gentamicin diluted solution was performed before placing of the semi-rigid implants.

In another case, a cross-over was discovered intra-operatively, and the prosthesis had to be removed. A dilator was then placed in the correct corporal space, and the contralateral corporal body was re-dilated more laterally. The implant was then placed in the newly dilated tract while maintaining the dilator in the contralateral cavity to prevent error. Once the implant was in the proper position, the dilator was removed, and the second implant was placed in the other corpora.

Table 1. Patients who underwent penile prosthesis implantation (2018-2022)

Implant type	**Number of cases**
Semi-rigid implant	28
Inflatable implant	7
Mean age (years)	59.5
Age range (years)	29-85
Causes of erectile dysfunction	**Number of cases n (%)**
Vasculogenic (cardiovascular, diabetes mellitus)	22 (77.1)
Anatomical and structural diseases (priapism and corporal fibrosis)	4 (11.4)
Peyronie's disease	2 (5.7)
Hypogonadism (post-orchiectomy)	1 (2.8)
Neurogenic (spinal cord injury)	1 (2.8)
Severity of erectile dysfunction	**Number of cases**
IIEF score 5-7	35

Post-operative events

There were no immediate postoperative complications, such as bleeding, hematoma, or infection, and no blood transfusions were required. Urethral catheters were removed one day post-operatively, with the exception of the case of urethral injury when the catheter was removed after five days. Hospital stay was one day.

One late complication was reported, in which a patient experienced a pseudo-malfunction of the implanted device one year after IPP. The patient felt a "hard pump" and could not inflate/deflate the device. This was managed non-surgically by applying very firm pressure to the pump bulb to move the valve disc into the inflate position. Once this was accomplished, the device inflated and deflated normally.

Three patients experienced pain that persisted for more than two weeks after the operation. On physical examination, there was no sign of infection or inflammation. The pain was localized to some area of the penile shaft and scrotum and slightly decreased after treatment with NSAIDs and opioids but responded well to Gabapentin. They were pain-free after six weeks and could discontinue Gabapentin.

Twenty-five patients (20 with semirigid implants and 5 with IPP) completed questionnaires about their satisfaction with the devices. The questionnaire from the Modified Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) was used as a tool to assess satisfaction with the treatment: 1) Are you satisfied with the improvement in sexual life, sensation, orgasm; 2) Is it easy to conceal device when not used; 3) Would you advise friends to undergo the same procedure.

Twenty-one (84%) patients reported that the devices were easy to use, provided good rigidity for intercourse, and resulted in normal sensation and orgasm. One patient was not satisfied with the semirigid implant because it was not rigid enough and underwent revision to IPP. Three men with persistent pain after implantation reported lower levels of satisfaction and were reluctant to perform sexual intercourse after six weeks.

Discussion

Surgical implantation of a penile prosthesis may be considered in patients who do not respond to pharmacotherapy or who prefer a permanent solution to their problem.[10] This study aimed to evaluate the outcome of PP implantation and also share experiences about implantation in complex cases.

Our results confirmed reports from previous studies showing that PP implantation was an effective treatment option for men with ED with low risk of complications and had a high level of patient satisfaction (92-100%).[11,12] Although the PP implantation generally results in very high satisfaction rates, less-than-perfect outcomes and post-operative dissatisfaction can still occur. Pre-operative counseling to identify patients who are at risk of dissatisfaction is also important.[4,13] This is the only way to connect pre-operative

expectation and post-operative reality. This context also played role in the selection of the appropriate device.

Infection

The most serious complication of penile prosthesis implantation is infection. The risk of infection with modern IPP in a virgin implantation has ranged from less than 1% to up to 4%.[14,15] However, there were no infections recorded in this series. Growing evidence suggests that the risk of infection associated with penile prosthesis has decreased over time due to improvement in both devices and surgical expertise. Higher-risk populations for infection include patients undergoing revision surgery, those with impaired host defenses (immunosuppression, diabetes mellitus, spinal cord injury), or those with penile corporal fibrosis.[12]

Diabetes and immunosuppression

In this study, 77% of patients had diabetes, which were controlled with an HbA1c level below 8.5 prior to the operation in all cases. No surgical site infections (SSI) or acute infections were detected in this study. Traditionally, diabetics have been considered a high-risk patient group for infection-related complications. Habous et al.[7] found that Hb1Ac levels were significantly related to a higher incidence of infection and proposed a threshold of 8.5% to predict infection with 80% sensitivity and 65% specificity. A large meta-analysis which included 9,041 diabetic patients and 36,517 non-diabetics showed that diabetes mellitus increases the incidence of penile prosthesis infection with an odds ratio of 1.53 (95% CI 1.15–2.04; p = 0.004).[16] However, data from a recent meta-analysis data changed this opinion, showing similar infection rates between diabetics, poorly controlled diabetics, and non-diabetics.[17] The diabetic issue is still controversial, debatable, and lacks consensus.

One kidney-transplanted recipient underwent PP implantation while taking immunosuppressive drugs, including Mycophenolatemofetil (Cellcept®) 500 mg twice daily, Tacrolimus (Prograf®) 1 mg twice daily, and Prednisolone 5 mg once daily. At the 1-month follow-up, the patient was doing well with no sign of surgical site infection. Cuellar et al followed 46 organ-transplanted patients for 2 years after PP implantation. In this series, the incidence of infection was no different than that of patients without organ transplant.[18] Sun et al found no significant increase in the infection rate after a 30-month follow-up of transplant recipients.[19] Based on these limited data, it is reasonable to consider transplant recipients on immunosuppression therapy as potentially good candidates for a penile prosthesis.

Revision

Revision due to system malfunction was observed in four cases. Revision rates due to system failure vary between centers, with recorded failure rates ranging from 15% at 5 years to 30-40% at 10 years.[20] Infection rates following revision surgery have been reported to be as high as between 10.0% and 13.3%, compared to 0.46% to 2.00% in virgin cases.[21] Infectious complications remain a significant concern in IPP revision surgery, with the risk of specific device infection showing a strong correlation with an increased risk based on the number of prior IPPs.[22] In 1996, Mulcahy et al. described a new protocol for the immediate replacement of infected IPPs, which involved the complete removal of the device and serial wound washout, followed by re-implantation of a new IPP.[23] This protocol was strictly followed in this series. Not only is the high infection rate a concern in this population, but overall complication rates, including intra-operative events (perforation, adjacent organ injury), post-operative corporal deformity, erosion, and patient dissatisfaction, are also high. In our study, the revision procedure required longer operative time than naïve cases. All components were delivered and carefully inspected for causes of malfunction. The explanted space was vigorously washed out before implantation. There were no surgical site infections or acute infections in this series, but for this special group of patients, a long-term follow-up period is necessary.

Corporal fibrosis

Three patients had corporal fibrosis from untreated Priapism. Two had an unknown etiology and one had Sickle cell disease. One patient had severe fibrosis from infection prior to implantation. PP implantation in corporal fibrosis is a significant surgical challenge. Due to the limited number of series there is no standard approach for this condition. Corporal fibrosis carries a high

risk for infection due to prolonged operative time and extensive tissue trauma, perforation during dilatation, adjacent organ injury and failure of the implantat.[24] Buranapitaksanti used the "Double Corporotomy Incision Technique"[25] to avoid false dilatation by a combination of sharp and blunt dissection.

Rossello 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. With this technique operative time and blood loss were reduced from 3.5 to 1.5 hours and 300 to 50 ml respectively in the first to the last case. All implants were successful with a semi-rigid implant being inserted without complication and a high level of satisfaction.

Peyronie's disease

Two patients with Peyronie's disease were implanted with semirigid implants. Penile prosthesis implantation is typically reserved for the treatment of Peyronie's disease in patients with ED, especially when they are non-responders to PDE5 inhibitors. The risk of complications such as infection and malformation is not increased in comparison to the general population.[26] Urethral injury was detected during the procedure in one patient, but implantation was not terminated. A urethral catheter was placed for 5 days, and there was no infection detected at the 2-week follow-up. Contemporary data suggest that termination and delayed implantation might not be necessary after injury.[27,28] One patient had an 80-degree dorsal curvature without ED. After a discussion about solutions for the deformity, such as plaque excision and grafting, plication, or shock wave therapy, he could not accept the consequences and risks of surgery, such as numbness, hourglass deformity, or shortening, and desired PP as a solution. After implantation with semirigid implants, the remaining curvature was less than 20 degrees, and both patients recorded a high level of satisfaction.

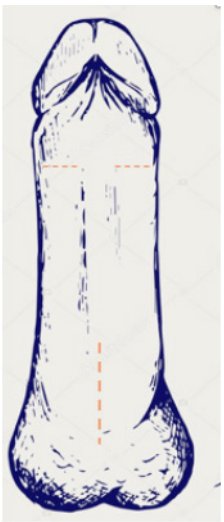


Figure 1. Double Corpototomy Incision Technique, Corporotomy performed along the red dotted lines.[25]

Conclusion

This 5-year review of PP implantation by a single surgeon shows a very low complication rate after surgery and a high level of patient satisfaction. Physical status of the patients needs to be evaluated before surgery and also all need to be counseled to ensure realistic, successful outcomes. In any high-risk group, implantation specialists should be prepared for complications using evidence-based data.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Scott FB, Bradley WE, Timm GW. Management of erectile impotence. Use of implantable inflatable prosthesis. Urology 1973;2:80-2.
2. Burnett AL, Nehra A, Breau RH, Culkin DJ, Faraday MM. Erectile dysfunction: AUA Guideline. J Urol 2018;200:633-41.
3. Hatzimouratidis K, Giuliano F, Moncada I, Muneer A, Salonia A, Verze P. EAU Guidelines on Erectile Dysfunction, Premature Ejaculation, Penile Curvature and Priapism [Internet]. [cited 2022 December 12]. Available from: https://d56bochluxqnz.cloudfront.net/media/16-Male-Sexual-Dysfunction_2017_web.pdf
4. Gopal L. Narang, Bradley D. Preoperative counseling and expectation management for inflatable penile prosthesis implantation. Transl Androl Urol 2017;6:S869-80.
5. Henry GD, Donatucci CF, Conners W. An outcomes analysis of over 200 revision surgeries for penile prosthesis implantation: A multicenter study. J Sex Med 2012;9:309-15.
6. Jackson G, Boon N, Eardley I, Kirby M, Dean J, Hackett G, et al. Erectile dysfunction and coronary artery disease prediction: evidence-based guidance and consensus. Int J Clin Pract 2010;64:848-57.

7. Habous M, Tal R, Tealab A, Soliman T, Nassar M, Mekawi Z, et al. Defining a glycated haemoglobin (HbA1c) level that predicts increased risk of penile implant infection. BJU Int 2018;121:293-300.
8. Culkin DJ, Exaire EJ, Green D, Soloway MS, Gross AJ, Desai MR, et al. Anticoagulation and antiplatelet therapy in urological practice: ICUD/AUA review paper. J Urol 2014;192:1026-34.
9. Wolf JS, Bennett CJ, Dmochowski RR, Hollenbeck BK, Pearle MS, Schaeffer AJ. Urologic Surgery Antimicrobial Prophylaxis Best Practice Policy Panel. Best practice policy statement on urologic surgery antimicrobial prophylaxis. J Urol 2008;1794:1379-90.
10. Antonini G, Busetto GM, Berardinis ED, Givannone R, Vicini P, Giudice FD, et al. Minimally invasive infrapubic inflatable penile prosthesis implant for erectile dysfunction: Evaluation of efficacy, satisfaction profile and complications. Int J Impot Res 2016;28:4-8.
11. Salonia A, Burnett AL, Graefen M, Hatzimouratidis K, Montorsi F, Mulhall JP, et al. Prevention and management of postprostatectomy sexual dysfunctions part 2: recovery and preservation of erectile function, sexual desire, and orgasmic function. Eur Urol 2012;62:273-86.
12. Hellstrom WJG, Motague DK, Moncada I, Carson C, Minhas S, Faria G, et al. Implants, mechanical devices, and vascular surgery for erectile dysfunction. J Sex Med 2010;7:501-23.
13. Masterson TA, Palmer J, Dubin J, Ramasamy R. Medical pre-operative considerations for patients undergoing penile implantation. Transl Androl Urol 2017;6:S824-9.
14. Trost L, Wanzek P, Bailey G. A practical overview of considerations for penile prosthesis placement. Nat Rev Urol 2016;13:33-4.
15. Mandava SH, Serefoglu EC, Freier MT, Wilson SK, Hellstrom WJG. Infection retardant coated inflatable penile prostheses decrease the incidence of infection: A systematic review and meta-analysis. J Urol 2012;188:1855-60.
16. Gon LM, Campos CCC, Voris BRI, Passeri LA, Fregonesi A, Riccetto CLZ. A systematic review of penile prosthesis infection and meta-analysis of diabetes mellitus role. BMC Urol 2021;21:35.
17. Christodoulidou M, Pearce I. Infection of Penile Prostheses in Patients with Diabetes Mellitus. Surg Infect 2016;17:2-8.
18. Cuellar DC, Sklar GN. Penile prosthesis in the organ transplant recipient. Urology 2001;57:138-41.
19. Sun AY, Babbar P, Gill BC, Angermeier KW, Montague DK. Penile Prosthesis in Solid Organ Transplant Recipients-A Matched Cohort Study. Urology 2018;117:86-8.
20. Carson CC, Mulcahy JJ, Govier FE. Efficacy, safety and patient satisfaction outcomes of the AMS 700CX inflatable penile prosthesis: results of a long-term multicenter study. J Urol 2000;164:376-80.
21. Montgomery BD, Lomas DJ, Zeigelmann MJ, Trost LW. Infection risk of undergoing multiple penile prostheses: an analysis of referred patient surgical histories. Int J Impot Res 2018;30:147-52.
22. Brant MD, Ludlow JK, Mulcahy JJ. The prosthesis salvage operation: immediate replacement of the infected penile prosthesis. J Urol 1996;155:155-7.
23. Mulcahy JJ. Long-term experience with salvage of infected penile implants. J Urol 2000;163:481-2.
24. Krughoff K, Bearelly P, Apoj M, Munarriz NA, Thirumavalavan N, Pan S, et al. Multicenter surgical outcomes of penile prosthesis placement in patients with corporal fibrosis and review of the literature. Int J Impot Res 2022;34:86-92.
25. Buranapitaksanti D, Penile prosthesis in severe corporal fibrosis: a history of a difficult case using the double corporotomy incision technique. Insight Urol 2022;43:167-70.
26. Wilson SK, Delk II JR. A new treatment for Peyronie's disease: modeling the penis over an inflatable penile prosthesis. J Urol, 1994;152:1121-3.
27. Sexton SJ , Granieri MA, Lentz AC. Survey on the Contemporary Management of Intraoperative Urethral Injuries During Penile Prosthesis Implantation. J Sex Med 2018;15:576-81.
28. Robert B, Grimberg DC, Lentz AC. Management of Urethral Injury During Penile Prosthesis Surgery. Curr Sex Health Rep 2020;12:62-7.

Original Article

Comparison of the quality of life between ileal conduit and orthotopic neobladder in post radical cystectomy bladder cancer male patients using the FACT-BL questionnaire

Napat Ditchaiwong[1], Supon Sriplakich[1], Thanakorn Booranachon-apha[2], Wasana Khampiwmar[2]

[1]Division of Urology, Department of Surgery, Faculty of Medicine, Chiang Mai University, Chiang Mai, [2]Division of Urology, Department of Surgery, Buddhachinaraj Hospital, Phitsanulok, Thailand

Keywords:
Urinary diversion, bladder cancer, quality of life, FACT-BL

Abstract

Objective: Radical cystectomy (RC) is standard treatment for bladder cancer. Removal of the bladder requires reconstruction of the lower urinary tract, a procedure that also has impact on the patient's quality of life (QoL). In Thailand, information pertinent to the level of the quality of life between ileal conduit and orthotopic neobladder is still limited. The objectives of this study are to evaluate the quality of life (primary outcome) and oncologic outcome (secondary outcome) of patients who underwent an Ileal Conduit (IC) or Orthotopic Neobladder (NB) using FACT-BL, a bladder-cancer-specific questionnaire.

Materials and Methods: One hundred and forty six patients underwent radical cystectomy and urinary diversion for bladder cancer from 2009 to 2019 at our institution. Out of these, 61 (42%) patients were asked to participate in this study. All 61, who were divided into two groups, 34 IC and 27 NB, completed the questionnaire, a survey response rate of 100%. Mean follow-up was 7 years 3 months.

Results: There were no statistically significant differences in ll FACT-G categories (PWB, SWB, EWB and FWB) between the two groups. Patients with neobladder had reported that they urinated more frequently than usual. Mean interest in sex was 49% in all patients and capability of maintaining an erection was 23%.
The mean total values of FACT-BL in IC and NB patients were 128.51 ± 15.51 and 126.70 ± 17.35, showing no significant difference.

Conclusion: Prinary diversion type does not appear to be associated with differential post-operative QoL and sexual satisfaction. There is a possibility that patients with neobladder urinate more frequently than before surgery but this did not reach statistical significance.

Insight Urol 2023;44(1):28-36. doi: doi: 10.52786/isu.a.69

Corresponding author: Supon Sriplakich

Address: Division of Urology, Department of Surgery, Faculty of Medicine, Chiang Mai University, Maharaj Nakorn Chiang Mai Hospital, 110 Intawaroros Road, Sriphum, Muang, Chiang Mai 50200, Thailand

E-mail: ssriplak@hotmail.com

Manuscript received: March 23, 2022

Revision received: May 28, 2023

Accepted after revision: June 2, 2023

Introduction

The 10th most common cancer in the world is bladder cancer. Bladder cancer is over four times more common in men than women and the sixth most frequent and ninth most deadly neoplasm.[1] Radical cystectomy (RC) is the standard treatment for localized muscle-invasive bladder cancer, high-risk non-muscle invasive cancers, or cancers resistant to intravesical chemotherapy.[2]

Once a patient has had a cystectomy, a urinary reconstruction is needed which may have specific problems related to the surgery, such as urine leakage, change of body image and loss of sexual interest. All prospective studies published after 2011 have shown neobladder to have superior QoL outcomes compared to other urinary diversion types. NB is more successful than IC in terms of physical functioning, role functioning, social functioning, global health status/QoL and financial expenditure.[3,4]

FACT-BL, the Functional Assessment of Cancer Therapy – Bladder, is a 39 item instrument developed to measure five domains in bladder cancer patients. This tool has recently become available for use in conjunction with FACT-G, and its coefficients of reliability and validity are uniformly high. The ability of this scale to discriminate patients on the basis of stage of disease, performance status rating (PSR), and hospitalization status supports its high level of sensitivity.[5]

Although these validated instruments are assumed to be useful, few studies in Thailand have compared the QoL of patients with an ileal conduit (IC) or an orthotopic neobladder (NB), using the FACT-BL questionnaire.[6]

In this study, we assessed the QoL of patients who underwent different forms of urinary diversions, using the Thai version of the FACT-BL questionnaire. We examined differences in Quality of Life between Ileal Conduit and Orthotopic Neobladder in post radical cystectomy bladder cancer male patients by using the FACT-BL questionnaire that assesses specific symptoms, such as trouble controlling urine, body image appearance, sexual function and interest.

Materials and Methods

Study design

One hundred and forty-six patients underwent radical cystectomy and urinary diversion for bladder cancer from 2009 to 2019 at our institution. Out of these, 85 (58%) patients were deceased at the time of this study and the remaining 61 were asked to participate in this study. All 61 patients answered the questionnaire giving a survey response rate of 100%. 18 (30%) patients answered the questionnaire at OPD and 43 (70%) patients answered the questionnaire by phone. Each patient completed a consent form. These patients included 34 with IC and 27 with NB. Mean follow-up was 86.9 months.

QoL was assessed using FACT-BL. This score was calculated from physical, social, emotional, and functional well-being, and a bladder cancer subscale. Higher FACT scores indicated a higher level of QoL. The questionnaire was translated into Thai by FACIT.org. Napat Ditchaiwong ("Investigator") has been granted license to use the Thai version of the FACT-Bl.

The medical records of each patient were reviewed. Clinical and demographic parameters including age, time after the procedure at survey, time in surgery, type of diversion, and final pathological status, were recorded.

The Research Ethics Committee of the Faculty of Medicine, Chiang Mai University approved this study (study number: SUR 2562-06927) (Figure 1).

Study setting

This study is a double-center study carried out at Maharaj Nakorn Chiang Mai Hospital (Chiang Mai University Hospital) and Buddhachinaraj Hospital, Thailand. These are teaching and referral hospitals.

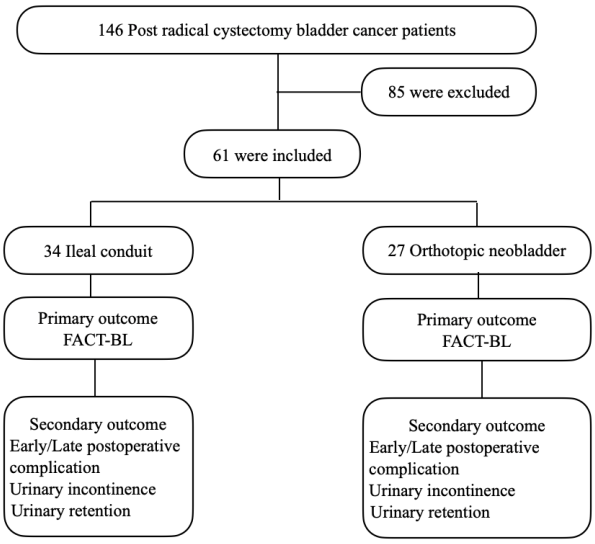


Figure 1. Flow diagram

Data collection and definitions

All data was collected from the hospital digital database, the Chiang Mai University registry database and the Buddhachinaraj Hospital database.

The 10-year data (2009-2019) was evaluated.

The primary outcome of the study, the quality of life, was calculated from the FACT-BL questionnaire.

The secondary outcome assessed the early/late postoperative complications, urinary incontinence and urinary retention

Statistical analysis

The categorical data is shown as number and percentage and is analyzed using Fisher's exact test. The continuous data (baseline characteristics) are shown as mean and standard deviation or median and interquartile range and are analyzed using Chi-square test for categorical variables. A p-value < 0.05 was used to denote statistically significant. The analysis was performed using STATA program version 14.0 (STATA corp, CS, TX, USA).

Results

Demographic and clinical features

The 61 patients who met the inclusion criteria were stratified into an IC group (n = 34) and an NB (n = 27) group (Table 1). There were significant differences in the numbers undergoing each operation type. Comparisons between the two groups showed no significant differences in age at surgery and survey, underlying disease and the follow up period. Patients undergoing NB were statistically significantly at a lower stage than IC (85.19% vs 58.82%).

12 (35%) of the 34 patients who underwent IC compared to 5 (18%) of the 27 patients with NB received systemic chemotherapy. There were no significant differences between these numbers.

Only one patient with IC had radiation therapy. Both groups of patients had different types of questionnaires due to COVID-19 situation. Most hospitals had preventative methods such as postponing follow up for disease stable patients.

Primary outcome

FACT-BL scores are shown in Table 2. Overall mean ± SD of FACT-BL was 127.71 ± 16.24. The mean ± SD of FACT-G in patients with IC and NB was 94.11 ± 12.87 and 93.49 ± 13.29, respectively, showing no significant differences. Both patient groups had high scores for EWB (25.20 ± 3.69 of total 28 points) and there was no significant difference between the groups. Total scores of bladder-cancer subscales were similar between each group.

The results of the bladder-cancer subscale questionnaire are shown in table 3 and table 4.

There were no significant differences in controlling urine between IC and NB. However, 22 (81%) out of 27 patients with NB reported that after surgery they urinate more frequently than usual, in comparison to 18 (52%) out of 34 patients with IC. 5 (15%) out of 34 and 8 (30%) out of 27 patients with IC and NB, respectively, feel it burns when they urinate these results were not significantly different. Half (50.8%) of post radical cystectomy patients have no interested in sex at all. 85% of IC and 67% of NB reported an inability to maintain an erection.

Feelings about the appearance of their bodies were not significantly different.

The questions, "I am embarrassed by my ostomy appliance" and, "caring for my ostomy appliance is difficult", was only on the questionnaire for IC patients. 70% of IC reported that they were not embarrassed by their ostomy appliance. Caring for their ostomy is found difficult in 73% of IC patients.

Secondary outcome

Oncological scores are shown in table 5.83% and 51% of patients had no early or late postoperative complications, respectively. There were no significant differences in early and late complications in both groups. Urinary incontinence and retention were reported only for NB.

68% and 96% of NB patients had no urinary incontinence or retention, respectively (Table 5).

Discussion

In this study, we used the Thai version of the FACT-BL for which we received licensure from FACIT.org. FACT-BL is a well-known respected questionnaire to assess differences in QoL among bladder cancer patients subjected to different types of urinary diversion.[7]

Dutta et al. used FACT-G in 72 patients with IC or NB and found no significant differences in total FACT-G scores between the groups which was the same as this study.8 However, they found

Table 1. Demographic and clinical features

Parameters	Total N=61	Type of diversion		P-value
		Ileal conduit (n=34)	Neobladder (n=27)	
Operation type n (%)				
Open RC	31 (50.82)	11 (32.35)	20 (74.07)	0.002
Lap RC	30 (49.18)	23 (67.65)	7 (25.93)	
Mean age at survey ± SD (years)	68.61 (8.82)	70.07±9.0	66.74±8.39	0.143
Mean age at surgery ± SD (years)	61.70 (9.40)	62.33±9.89	60.93±8.88	0.568
Median month at Follow up (IQR)	86.89 (62.27)	94 (56)	67(110)	0.135
U/D n (%)				0.204
0 = No	18 (29.63	10 (31.25)	8 (29.63)	
1 = DM	2 (7.41)	1 (3.13)	2 (7.41)	
2 = HT	7 (25.93)	7 (21.88)	7 (25.93)	
3 = Anemia	0 (0.00)	2 (6.25)	0 (0.00)	
5 = CVD	0 (0.00)	1 (3.13)	0 (0.00)	
7 = Renal disease	1 (3.70)	5 (15.63)	1 (3.70)	
10 = Previous Surgery	0 (0.00)	2 (6.25)	0 (0.00)	
12 = Multiple diseases	9 (33.33)	4 (12.50)	9 (33.33)	
PT stage n (%)				
0	1 (1.64)	0 (0.00)	1 (3.70)	0.443
1 = < T2	18 (29.51)	14 (41.18)	4 (14.81)	0.046
2 = T2	16 (59.26)	13 (38.24)	16 (59.26)	0.126
3 = T3	5 (18.52)	2 (5.88)	5 (18.52)	0.224
4 = T4	1 (3.70)	5 (14.71)	1 (3.70)	0.214
PN stage n (%)				
0 = N0	54 (88.52)	31 (91.18)	23 (85.19)	0.689
1 = N1	6 (9.84)	3 (8.82)	3 (11.11)	1.000
3 = N3	1 (1.64)	0 (0.00)	1 (3.70)	0.443
PM stage n (%)				-
M0	61 (100.00)	34 (100.00)	27 (100.00)	
M1	0 (0.00)	0 (0.00)	0 (0.00)	
Systemic chemo n (%)				0.064
0 = No	44 (72.13)	22 (64.71)	22 (81.48)	
1 = Neoadjuvant	10 (16.39)	9 (26.47)	1 (3.70)	
2 = Adjuvant	7 (11.48)	3 (8.82)	4 (14.81)	
Post op radiation therapy n (%)				1.000
0 = No	60 (98.36)	33 (97.06)	27 (100.00)	
1 = Yes	1 (1.64)	1 (2.94)	0 (0.00)	
Questionnaire n (%)				0.046
1 = Paper	18 (29.51)	14 (41.18)	4 (14.81)	
2 = Phone call	43 (70.49)	20 (58.82)	23 (85.19)	

RC = radical cystoprostatectomy, IC = ileal conduit, NB = neobladder, DM = diabetes mellitus, HT = hypertension, CVD = cardiovascular disease, multiple disease = more than 1 disease

that patients with NB had significantly better EWB and FWB than IC. In contrast to our study in which there were no differences between the groups in any domains of FACT-G.

Mansson et al. compared the QoL of 64 patients with a continent reservoir or NB using FACT-BL and observed no differences in any domain of FACT-G between the two groups.[6]

In their study, patients with a continence reservoir had significantly less trouble controlling urine and patients with NB had a significantly better appreciation of their body appearance. In our series, both groups of patients had no differences in controlling their urine and appreciation of their body appearance.

Table 2. Primary outcome (FACT-BL in the diversion groups)

Function (maximum)	Total N=61	Type of diversion		P-value
		Ileal conduit (n=34)	Neobladder (n=27)	
PWB (28)				0.819
Mean (SD)	25.20 (3.69)	25.29 (3.82)	25.07 (3.59)	
Median (p25, p75)	27 (24, 28)	27 (24, 28)	26 (23, 28)	
SWB (28)				0.509
Mean (SD)	22.80 (4.79)	23.17 (4.42)	22.34 (5.27)	
Median (p25, p75)	23.30 (20, 26.8)	23.65 (21, 26.8)	23 (18, 26.8)	
EWB (24)				0.641
Mean (SD)	22.36 (3.42)	22.18 (3.51)	22.59 (3.35)	
Median (p25, p75)	23 (21, 24)	22.5 (21, 24)	23 (21, 24)	
FWB (28)				0.993
Mean (SD)	23.48 (4.49)	23.47 (4.49)	23.48 (4.57)	
Median (p25, p75)	24 (22, 28)	24.5 (20, 28)	24 (22, 28)	
FACT-G (108)				0.855
Mean (SD)	93.84 (12.95)	94.11 (12.87)	93.49 (13.29)	
Median (p25, p75)	95 (86, 102)	96.5 (86, 101)	94 (84, 105)	
Bladder-specific subscale (48)				0.415
Mean (SD)	33.87 (5.62)	34.40 (5.32)	33.21 (6.01)	
Median (p25, p75)	34.8 (31, 38)	35 (32, 38)	33.6 (28.8, 37.2)	
FACT-BL TOI (104)				0.616
Mean (SD)	82.54 (10.73)	83.16 (10.64)	81.76 (10.99)	
Median (p25, p75)	84 (75, 91)	86.5 (75, 92)	80.8 (75, 90.2)	
FACT-BL (156)				0.6693
Mean (SD)	127.71 (16.24)	128.51 (15.51)	126.70 (17.35)	
Median (p25, p75)	129.2 (119, 139)	131 (119, 138)	128.2 (115.6, 142.4)	

PWB = physical well-being, SWB = social/family well-being, EWB = emotional well-being, FWB = functional well-being, FACT-G = functional assessment of cancer therapy – general, FACT-BL = functional assessment of cancer therapy – bladder

We found that our NB patients urinated significantly more frequently than usual.

Urinary incontinence following orthotopic NB replacement is a common finding in NB patients.[9] In contrast to stoma patients, IC patients easily manage their urine by using a urine bag for diversion all the time. This situation makes control of urine more easily manageable in comparison to NB patients.

With regard to external body scores, Bjerre BD et al. and Kikuchi et al. found that IC patients had a significantly poorer body image than those with NB.[10,11] This was in contrast to our study which found that both groups had no differences in their perception of body image.

Erectile dysfunction and sexual dysfunction in men are common after cystectomy and urinary diversion. Radical cystectomy without nerve sparing surgery also causes other factors that affect sexual function such as psychological issues, age, and health-related competing risks for ED. However, body image, partner response, and change in life course and sexual priorities, have received less attention.[12] Our study found that half of our patients were not interested in sex and a small majority of them were unable to maintain an erection. It may be important to counsel the patient about their sexual life after radical cystectomy.

Daytime and nighttime incontinence is common in NB patients following surgery, but improves considerably with time.[13] In our study, 32% of NB (median time at follow up 7 years 3 months) experienced urinary incontinence.

In males undergoing radical cystectomy with NB, retention requiring catheterization to void is uncommon. Freedom from any catheterization or retention at 5 years after RC was 77% and 88%, respectively.[14] In our study, 3.7% of NB (median month at follow up 7 years 3 months) had urinary retention.

Table 3. Answer to bladder-cancer subscale question

Bladder-specific subscale	Total N=61 n (%)	Type of diversion	
		Ileal conduit (n=34) n (%)	Neobladder (n=27) n (%)
BL1 I have trouble controlling my urine			
0 = Not at all	24 (39.34)	16 (47.06)	8 (29.63)
1 = A little bit	9 (14.75)	5 (14.71)	4 (14.81)
2 = Somewhat	12 (19.67)	6 (17.65)	6 (22.22)
3 = Quite a bit	10 (16.39)	3 (8.82)	7 (25.93)
4 = Very much	6 (9.84)	4 (11.76)	2 (7.41)
BL2 I urinate more frequently than usual			
0 = Not at all	21 (34.43)	16 (47.06)	5 (18.52)
1 = A little bit	15 (24.59)	8 (23.53)	7 (25.93)
2 = Somewhat	8 (13.11)	4 (11.76)	4 (14.81)
3 = Quite a bit	9 (14.75)	2 (5.88)	7 (25.93)
4 = Very much	8 (13.11)	4 (11.76)	4 (14.81)
BL3 It burns when I urinate			
0 = Not at all	48 (78.69)	29 (85.29)	19 (70.37)
1 = A little bit	6 (9.84)	2 (5.88)	4 (14.81)
2 = Somewhat	2 (3.28)	1 (2.94)	1 (3.70)
3 = Quite a bit	2 (3.28)	1 (2.94)	1 (3.70)
4 = Very much	3 (4.92)	1 (2.94)	2 (7.41)
BL4 I am interested in sex			
0 = Not at all	31 (50.82)	20 (58.82)	11 (40.74)
1 = A little bit	6 (9.84)	3 (8.82)	3 (11.11)
2 = Somewhat	18 (29.51)	7 (20.59)	11 (40.74)
3 = Quite a bit	3 (4.92)	3 (8.82)	0 (0.00)
4 = Very much	3 (4.92)	1 (2.94)	2 (7.41)
BL5 I am able to have and maintain an erection			
0 = Not at all	47 (77.05)	29 (85.29)	18 (66.67)
1 = A little bit	6 (9.84)	0 (0.00)	6 (22.22)
2 = Somewhat	4 (6.56)	2 (5.88)	2 (7.41)
3 = Quite a bit	4 (6.56)	3 (8.82)	1 (3.70)
4 = Very much	0 (0.00)	0 (0.00)	0 (0.00)
C7 I like the appearance of my body			
0 = Not at all	3 (4.92)	3 (8.82)	0 (0.00)
1 = A little bit	(0.00)	0 (0.00)	0 (0.00)
2 = Somewhat	10 (16.39)	7 (20.59)	3 (11.11)
3 = Quite a bit	19 (31.15)	11 (32.35)	8 (29.63)
4 = Very much	29 (47.54)	13 (38.24)	16 (59.26)
C8 I am embarrassed by my ostomy appliance			-
0 = Not at all	24 (70.59)	24 (70.59)	
1 = A little bit	2 (5.88)	2 (5.88)	
2 = Somewhat	5 (14.71)	5 (14.71)	
3 = Quite a bit	1 (2.94)	1 (2.94)	
4 = Very much	2 (5.88)	2 (5.88)	
C9 Caring for my ostomy appliance is difficult			-
0 = Not at all	9 (26.47)	9 (26.47)	
1 = A little bit	11 (32.35)	11 (32.35)	
2 = Somewhat	10 (29.41)	10 (29.41)	
3 = Quite a bit	3 (8.82)	3 (8.82)	
4 = Very much	1 (2.94)	1 (2.94)	

Table 4. Bladder-cancer subscale question (Yes vs No)

Bladder-specific subscale	Total N=61 n (%)	Type of diversion		P-value
		Ileal conduit (n=34) n (%)	Neobladder (n=27) n (%)	
BL1 I have trouble controlling my urine				0.196
0 = Not at all	24 (39.34)	16 (47.06)	8 (29.63)	
1 - 4	37 (60.66)	18 (52.94)	19 (70.37)	
BL2 I urinate more frequently than usual				0.030
0 = Not at all	21 (34.43)	16 (47.06)	5 (18.52)	
1 - 4	40 (65.57)	18 (52.94)	22 (81.48)	
BL3 It burns when I urinate				0.212
0 = Not at all	48 (78.69)	29 (85.29)	19 (70.37)	
1 - 4	13 (21.31)	5 (14.71)	8 (29.63)	
BL4 I am interested in sex				0.202
0 = Not at all	31 (50.82)	20 (58.82)	11 (40.74)	
1 - 4	30 (49.18)	14 (41.18)	16 (59.26)	
BL5 I am able to have and maintain an erection				0.126
0 = Not at all	47 (77.05)	29 (85.29)	18 (66.67)	
1 - 4	14 (22.95)	5 (14.71)	9 (33.33)	
C7 I like the appearance of my body				0.248
0 = Not at all	3 (4.92)	3 (8.82)	0 (0.00)	
1 - 4	58 (95.08)	31 (91.18)	27 (100.00)	

Neobladder patient did not answer for C8, C9 question

Table 5. Bladder-cancer subscale question (Yes vs No)

Oncological outcome	Total N=61 n (%)	Type of diversion		P-value
		Ileal conduit (n=34) n (%)	Neobladder (n=27) n (%)	
Early complication				0.974
0 = No	51 (83.61)	28 (82.35)	23 (85.19)	
2 = Bowel ileus	1 (1.64)	1 (2.94)	0 (0.00)	
3 = Bowel injury	2 (3.28)	1 (2.94)	1 (3.70)	
6 = Bowel obstruction	1 (1.64)	1 (2.94)	0 (0.00)	
7 = Wound Complication	3 (4.92)	1 (2.94)	2 (7.41)	
8 = Multi	3 (4.92)	2 (5.88)	1 (3.70)	
Late complication				0.225
0 = No	47 (77.05)	26 (76.47)	21 (77.78)	
1 = Parastromal hernia	3 (4.92)	3 (8.82)	0 (0.00)	
2 = Stone	2 (3.28)	0 (0.00)	2 (7.41)	
3 = UTI	3 (4.92)	2 (5.88)	1 (3.70)	
6 = Anastomatic stricture	4 (6.56)	1 (2.94)	3 (11.11)	
7 = Bowel obstruction	1 (1.64)	1 (2.94)	0 (0.00)	
8 = Multi	1 (1.64)	1 (2.94)	0 (0.00)	
Urinary incontinence				-
0 = No	17 (68.00)	0 (0.00)	17 (68.00)	
1 = Yes	8 (32.00)	0 (0.00)	8 (32.00)	
Urinary retention				-
0 = No	26 (96.30)	0 (0.00)	26 (96.30)	
1 = Yes	1 (3.70)	0 (0.00)	1 (3.70)	

UTI = urinary tract infection

In one study it was shown that in contrast to males, females undergoing continuous urinary diversion had worse FACT-BL scores in comparison with those with a neobladder.[15]

One point to mention is that the diapers necessary for neobladder patients are personal expenses while the ostomy bag in an ileal conduit patient is sponsored by the government.

There are several limitations of this study including firstly it was a cross-sectional study. The decision to perform any type of urinary diversion depends upon many considerations, including patient factors such as co-morbidity, age, body build and surgeon preferences. 32 (72%) out of 44 Maharaj Hospital patients underwent IC while 15 (88%) out of 17 Buddhachinaraj Hospital patients underwent NB. The type of surgery was dependent on the surgeon's decision. However, there were no differences in demographic and clinical features between groups, with the exception of operation type (open or laparoscopic). All radical cystectomy performed at Buddhachinaraj Hospital is by open procedure, therefore 74% of NB are open surgery.

Second, both groups of patients had different methods of completion of the questionnaires. Due to the COVID-19 situation, most hospitals had preventive methods of postponing follow up for disease stable patients, and answering the FACT-BL questionnaire face to face or by phone call may alter the results.

Third, this study was only reported for male patients and other studies have found that interest in sex and body appearance may differ in female patients.

Conclusions

In conclusion, based on data from this cross-sectional, non-randomized study with a small sample size, males treated with Ileal Conduit or Neobladder do not appear to experience differential post-operative QoL or sexual satisfaction. However, Neobladder patients seem to complain that they urinate more frequently than before surgery. Further randomized prospective studies are needed.

Acknowledgement

Our authors would like to thank Mrs. Landra Tedstrom, Chiang Mai University English Language Team, for language editing.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
2. NCCN guidelines version 1.2022 bladder cancer [Internet]. [cited 2022 February 22]. Available from: http://www.nccn.org/ professionals/physician_gls/pdf/bladder.pdf
3. Ghosh A, Somani BK. Recent trends in postcystectomy health-related quality of life (QoL) favors neobladder diversion: Systematic review of the literature. Urology 2016;93:22-6.
4. Singh V, Yadav R, Sinha RJ, Gupta DK. Prospective comparison of quality-of-life outcomes between ileal conduit urinary diversion and orthotopic neobladder reconstruction after radical cystectomy: A statistical model. BJU Int 2014;113:726-32.
5. Cella DF, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, et al. The functional assessment of cancer therapy scale: development and validation of the general measure. J Clin Oncol 1993;11:570-9.
6. Mansson A, Davidsson T, Hunt S, Mansson W. The quality of life in men after radical cystectomy with a continent cutaneous diversion or orthotopic bladder substitution: is there a difference? BJU Int 2002;90:386-90.
7. Elbadry MS, Ali AI, Hassan A, Clement KD, Hammady AR, Abdbelaal A, et al. The relationship between type of urinary diversion and quality of life after radical cystectomy: Ileal conduit versus orthotopic bladder. BJUI Compass 2020;1:133-8.
8. Dutta SC, Chang SC, Coffey CS, Smith JA, Jr., Jack G, Cookson MS. Health related quality of life assessment after radical cystectomy: comparison of ileal conduit with continent orthotopic neobladder. J Urol 2002;168:164-7.
9. Steers WD. Voiding dysfunction in the orthotopic neobladder. World J Urol 2000;18:330-7.
10. Bjerre BD, Johansen C, Steven K. Health-related quality of life after cystectomy: bladder substitution compared with ileal conduit diversion. A questionnaire survey. Br J Urol 1995;75:200-5.
11. Kikuchi E, Horiguchi Y, Nakashima J, Ohigashi T, Oya M, Nakagawa K, et al. Assessment of Long-term quality of life using the FACT-BL questionnaire in patients with an ileal conduit, continent reservoir, or orthotopic neobladder. Jpn J Clin Oncol 2006; 36:712-6.

12. Modh R, Mulhall J, Gilbert S. Sexual dysfunction after cystectomy and urinary diversion. Nat Rev Urol 2014;11:445-53.
13. Nayak A, Cagiannos I, Lavallée L, Morash C, Hickling D, Mallick R, et al. Urinary function following radical cystectomy and orthotopic neobladder urinary reconstruction. Can Urol Assoc J 2018;12:181-6.
14. Ghodoussipour S, Ladi S, Jiang D, Lifton J, Ahmadi H, Wayne K, et al. Predictors of need for catheterisation and urinary retention after radical cystectomy and orthotopic neobladder in male patients. BJU Int 2021;128:304-10.
15. Gacci M, Saleh O, Cai T, Gore JL, D'Elia C, Minervini A, et al. Quality of life in women undergoing urinary diversion for bladder cancer: results of a multicenter study among long-term disease-free survivors. Health Qual Life Outcomes 2013;11:43.

Invited Review Article

Review of various surgical approaches for varicocele management

Supanut Lumbiganon[1], Muhammed Hammad[2], David W. Barham[2], Faysal A. Yafi[2]

[1]Department of Surgery, Faculty of Medicine, Khon Kaen University, Thailand, [2]Department of Urology, University of California, Irvine, CA, United States

Keywords:
Varicocele, scrotum, venous plexus, varicocelectomy

Abstract

Varicocele is one of the most common correctable causes of male infertility. Varicocele can also cause scrotal pain or discomfort. Treatment of varicocele is proved to have benefits in terms of fertility and pain. There are many treatment options for varicocele. This review aims to describe the treatment procedures and determine the outcomes, advantages and disadvantages for each treatment option.

Insight Urol 2023;44(1):37-42. doi: 10.52786/isu.a.70

Introduction

Varicocele refers to the abnormal dilatation of the pampiniform plexus[1] which has been associated with scrotal pain, male-factor infertility, and hypogonadism. Nagler et al.[2] reported a 37% incidence of varicocele in infertile men compared to 13% in the general population. Another report by Clavijo et al.[3] found an average 15% prevalence of varicocele in healthy men compared to 45% of men presenting with primary infertility. Furthermore, up to 80% of men seeking care for secondary infertility have a varicocele.[3] Therefore, the treatment of a varicocele should be considered for men attempting to conceive who have palpable varicocele (s), infertility, and abnormal semen parameters, except for azoospermic men.[4] Other proposed indications for varicocele treatment include men with clinical varicocele, testosterone deficiency, chronic persistent and refractory testicular pain associated with the varicocele.[5]

There are many accepted treatment options for varicocele management including retroperitoneal, inguinal, or subinguinal varicocelectomy. Microscopic assistance is often used for the inguinal and subinguinal approaches. Laparoscopic varicocelectomy and the embolization of the spermatic vein are also accepted treatment options. We aim to review the current treatment options for varicocele and to determine the outcomes, advantages, and disadvantages of each treatment option.

Methods

We conducted a narrative review of operative procedures for varicocele treatment options and outcomes. We searched for standard textbooks and previous articles to describe these procedures. To extract the outcomes of these operative procedures, we conducted a literature search using PubMed and Google Scholar using combinations of the search terms "varicocele", "treatment", and "outcomes."

Corresponding author: Faysal A. Yafi
Address: Department of Urology, University of California, Irvine, CA, USA
E-mail: fyafi@hs.uci.edu
Manuscript received: April 19, 2023
Revision received: May 20, 2023
Accepted after revision: June 2, 2023

Selection of articles

We selected articles based on the following criteria:

- They were written in English.
- They reported the outcomes of varicocele treatment options.
- They were published between 1990 and 2022.

We excluded studies that were not relevant to our review, including studies on non-surgical treatments and studies that did not report outcomes.

Data extraction

We extracted data from the selected articles using a standardized data extraction form. We extracted the following information from each article:

- Study design
- Sample size
- Age and sex of participants
- Intervention type
- Follow-up period
- Outcome measures
- Results

We also extracted information on any adverse events reported in the studies. We included the selected references in the narrative review for additional information. We also checked the reference lists of these articles for additional relevant studies.

Surgical techniques

Microsurgical subinguinal varicocelectomy

Subinguinal varicocelectomy is currently one of the most popular techniques used to treat varicocele. An approximately three cm transverse skin incision is made just below the superficial inguinal ring. The subcutaneous tissue, Camper, and Scarpa's fascia are dissected. The spermatic cord is grasped with a Babcock clamp and delivered out to the level of the wound. The external and internal spermatic fascia are divided and a Penrose drain can be passed around the remaining cord structures to help lift up the cord into the operative field. An operating microscope with 8x to 25x magnification can be used[6] to obtain better visualization and identification of the fine vascular and lymphatic structures. A Micro-Doppler ultrasound can be used to identify and preserve the arterial anatomy. Papaverine irrigation is beneficial to induce vasodilation and further aid in arterial identification. The goal of the operation is to ligate all dilated veins while preserving the arterial and lymphatic anatomy. The veins can be ligated with silk ties or small clips.

An inguinal varicocelectomy can be performed using a similar technique; however, the incision is higher over the inguinal canal. The external oblique must be divided, thus creating greater morbidity with the operation. Lee et al. found men undergoing inguinal varicocelectomy had more postoperative pain compared to the subinguinal approach.[7] The main benefit of the inguinal approach compared to the subinguinal approach lies in the anatomy of the pampiniform plexus, as there are fewer branches of the external spermatic vein in the inguinal canal. Having fewer vessels to ligate may be preferable to many surgeons. Studies of varicocele anatomy suggest that access to and ligation of low inguinal and gubernacular veins may cause fewer varicocele recurrences[8] but encountering more veins may result in a more difficult procedure and longer operative time.[9]

A microsurgical subinguinal varicocelectomy offers good outcomes in terms of sperm parameters. The highest pregnancy rate (44.75%) was achieved from this approach.[10] The overall complication rates are lowest with microscopic varicocelectomy (< 5%) compared to laparoscopic (8-12%) and open retroperitoneal (5-30%) varicocelectomy.[11] Microscopic dissection and identification of lymphatic vessels lead to a lower hydrocele rate which is reported to be lowest (0.72%) with microscopic surgery compared to other conventional techniques (7.47%-7.58%).[10,12]

Wu et al. developed a modification of the subinguinal varicocelectomy where the spermatic cord is mobilized and gently 'pulled' distally.[13] This technique affords the convalescent benefit of a subinguinal approach, but also a more proximal dissection on the spermatic cord where there is less branching of the veins. The study enrolled 52 male patients with varicocele, with 26 patients undergoing the conventional microscopic subinguinal varicocelectomy and the other 26 patients undergoing the novel approach of treatment. The results showed that the novel approach had a shorter operative time and required the ligation of fewer vein branches compared to the conventional method. There was no significant difference

in the number of testicular arteries or lymphatic ducts between the two groups. The incidence of postoperative complications was similar for both groups. The authors concluded that the novel approach is a safe and effective method of varicocele treatment and can significantly reduce the number of internal veins to ligate and shorten the operating time without increasing complications.

Laparoscopic spermatic vein ligation

Laparoscopic management of varicocele has gained increasing acceptance over the last few decades.[14] The laparoscopic view offers great exposure to the posterior abdominal wall, particularly at the deep inguinal ring. The procedure is performed under general anesthesia with the patient placed in a supine position. One camera port and two instrument ports are usually sufficient. There are several locations of port placement, but the main objective is to have a clear vision and triangulate the internal inguinal ring. Port sizes can vary depending on surgeon preference and the size of the available equipment. However, a 5 mm trocar usually allows testicular vein clipping. The patient is then placed in a slight reverse Trendelenburg position. The internal inguinal ring and internal spermatic vessels are identified. The overlying peritoneum is opened to clearly expose the spermatic vessels. The pulsating artery is separated from the darker testicular vein[15] and the vein is ligated with Hem-o-lok or metallic clip and can then be divided.

The testicular vein in this part tends to be larger than the inguinal or subinguinal area, and the magnification from laparoscopic equipment contributes to the advantages of this procedure. The ability to perform bilateral varicocelectomy simultaneously compared to separate incisions with an open approach is also a benefit of the laparoscopic approach. A potentially longer hospital stay and treatment costs are drawbacks of this approach.[11]

The laparoscopic approach offers a lower pregnancy rate (27.5%) compared to other treatment methods (44.8% for microscopic subinguinal, 41.8% for microscopic inguinal, 31.9% for embolization and 30% for non-microscopic inguinal approach).[10] The recurrence rate (3%-15%) is lower than in a conventional open approach (9%-45%) but higher than in microscopic approaches (0%-2%).[11] Hydrocele formation is greater than with microscopic surgery (7.57 vs 0.72%).[10,16] Rizkala et al. demonstrated that the use of lymphatic sparing laparoscopic varicocelectomy had a lower hydrocele formation rate compared to plain laparoscopic varicocelectomy (4.5% vs 43.3%).[17]

Traditional open approaches

In 1949, Palomo described the open retroperitoneal approach for the treatment of varicocele.[18] The procedure involves an en-bloc section of the testicular vascular bundle. The modification of arterial and lymphatic sparing techniques has followed since then.

The concept of the procedure is to enter the retroperitoneal space by incision at the area of the internal inguinal ring, then split abdominal muscle to identify the internal spermatic vein and artery near the ureter. The advantages of this procedure are that only one or two large veins can be found at this level, also the artery has not branched yet and often separates from the vein. These anatomic features make it technically an easier procedure. Disadvantages are higher recurrence rate and hydrocele formation.[19]

The benefits of the traditional open Palomo procedure are the low cost, and that the ligation is high enough to avoid multiple branching veins but the collateral veins that branch out of the bundle inferior to the operating field in the procedure cannot be carried out, which can lead to a higher recurrence rate. Testicular atrophy after ligation of the testicular artery was rarely described. It also has a higher incidence of varicocele recurrence and hydrocele formation than any other treatment method.[11]

The inguinal approach procedure is easier than the retroperitoneal approach in obese patients and the ability to ligate more collateral external spermatic veins are the advantages of this procedure in terms of varicocele recurrence but the Ilioinguinal nerve should be identified and carefully preserve as the inguinal canal has to be open in this method.

Traditional open approaches offer a lower pregnancy rate than microscopic approaches (30% vs 41.8%-44.8%).[10,11] They also cause a higher recurrence rate and hydrocele formation.[12]

Embolization

Endovascular approaches for the treatment of varicocele involve venography to identify the internal spermatic and collateral veins with subse-

quent venous occlusion by various occlusion and embolization techniques.[20] For a left-sided varicocele, the right common femoral vein approach is technically easier to access the left internal spermatic vein. The endovascular catheter is passed through the inferior vena cava into the left renal vein and the gonadal vein. However, an internal jugular or basilic vein approach is preferable for right internal spermatic vein access because the acute angle of the gonadal vein and the inferior vena cava is difficult to navigate.[20] The catheter tip is placed at the junction of the internal spermatic vein and the pampiniform plexus and a venogram is performed to identify the collateral pattern. The choices of embolizing agents include solid embolics such as coils and vascular plugs. Liquid embolics such as sclerosant sodium tetradecyl sulfate and glue are also used.[20]

Technical successful embolization is defined as cessation of blood flow as demonstrated by intraoperative imaging. The treatment of right-sided varicocele has a technical failure rate as high as 49% in some reports[21,22] with an overall treatment failure of 13%.[23] Hydroceles are not typically seen in this approach while recurrence rates are low (1.9%-9.3%) comparable to the microsurgical technique (2.07%-9.47%).[10] Pregnancy rates (31.93%) are inferior to other microscopic approaches (41.78%-44.75%).[11]

Discussion

Varicocele is a common condition that can result in infertility and testicular pain. There are several treatment options available, and each technique has its own advantages and disadvantages. In determining the best option, surgeons must consider operative time and cost, pain resolution, fertility/pregnancy/semen parameters, and complications.

Surgery time and cost

A randomized trial comparing open, laparoscopic, and microsurgical varicocele treatment found that the operation time is usually longer in the microscopic group compared to laparoscopic and open surgery groups.[12] The laparoscopic approach had the highest treatment cost followed by microscopic and open approaches. Al-Kandari et al. reported the treatment cost of unilateral and bilateral varicocelectomy for 1) inguinal approach; $1800 and $2100 2) microscopic subinguinal approach; $2400 and $3000 3) laparoscopic approach; $2700 and $3600, respectively.[12] Based on pregnancy outcome, percutaneous embolization was the least cost-effective method (approximately 7300 Canadian dollars per pregnancy) compared to microsurgical varicocelectomy, the most cost-effective method (approximately 5402 Canadian dollars per pregnancy).[24]

Fertility and semen parameters

There was significant improvement of semen parameters in all open, laparoscopic, and microsurgical groups but no differences in degree among them.[12] A review article from Diegidio et al. concluded that microsurgical subinguinal or inguinal techniques offer the best outcomes since pregnancy rates were highest.[10] Most of the articles in this review report improved sperm parameters. Bebar et al.[25] found 43% compared to 51% improvement of sperm parameters by using Palamo and laparoscopic techniques respectively. Zampieri et al. reported 40.6% and 58.3% of patients had normalization of semen parameters by treatment of varicocele laparoscopically without and with the arterial preserving procedure, respectively.[26] Improvement in testosterone level and testicular size were seen but no comparison between each technique was shown. Meta-analysis in 2015 reported significant improvement in pregnancy rate with inguinal microsurgery, subinguinal microsurgery, open inguinal, and laparoscopic technique compared to expectant treatment (Odds ratio 3.48, 2.68, 2.92 and 2.90, respectively).[27] Inguinal microsurgery showed improvement in sperm density and motility compared with retroperitoneal open surgery.[27] A systematic review and meta-analysis in 2020 concluded that microsurgical varicocelectomy provides the greatest benefit to most patients in terms of higher spontaneous pregnancy rate and improvement of sperm parameters compared to laparoscopic or open varicocelectomy.[28] Percutaneous embolization had lower pregnancy rates than microsurgical varicocelectomy and there was a recommendation against it as a first-line treatment for varicocele in men with infertility.[20]

Complications

The microscopic group also had lower postoperative hydrocele and recurrent varicocele compared to the laparoscopic and open groups.[12]

A review from Diegidio et al. found that both microscopic inguinal and subinguinal techniques had lower hydrocele formation rates compared to open and laparoscopic approaches.[10] While the laparoscopic technique had the highest surgical complications.

Subinguinal and inguinal microsurgery outperformed retroperitoneal open surgery and lower than laparoscopic approach in terms of recurrence.[10,27] Inguinal microsurgery and subinguinal microsurgery also had lower overall complication rates compared with retroperitoneal open surgery while laparoscopic approach had more reported complications than other techniques.[10,27]

Diamond et al.[29] reported 10 years of varicocele treatment experience in children and adolescents. Although the laparoscopic approach had the highest success rate (100%) compared to Palamo (93%), Ivanissevich (69%) and subinguinal approach (69%), a higher hydrocele rate was seen in the laparoscopic approach. Artery sparing procedure decreased hydrocele formation.

For the embolization technique, technical failures are rare for left-sided varicocele but can be as high as 49% for right-sided varicocele. A meta-analysis from Cayan et al. reported an overall technical failure rate of 13%.[23] Theoretically, intra-operative venography during embolization can identify venous anastomosis variants, which thought to be the cause of recurrence in other surgical treatments but the literature reveals a wider range of recurrence rates (0%-24%) compared to 0%-3% for microsurgical varicocelectomy.[20]

Lurvey et al.[30] reported incidences of hydrocele to be 4.9%, 8.1%, and 5%; retreatment rates of 1.5%, 3.4%, and 9.9% when treated by open, laparoscopic, and percutaneous embolization techniques, respectively in varicocele patients under 19 years. The outcomes may be slightly different from the adult population since pediatric urologists may not be familiar with microscopic approaches, which makes microsurgical approaches account for only 2% of open varicocelectomy.[31]

Pain resolution

Approximately 2-10% of patients with varicocele complain about testicular pain. Al-Gadheeb et al. report 83.3% pain relief after microscopic subinguinal varicocelectomy. A significantly better pain relief is seen in patients with unilateral symptoms.[32] A systematic review and meta-analysis from Lundy et al. found that 75%, 76%, 85%, and 90% of patients had partial or complete improvement of pain after undergoing varicocelectomy by inguinal, retroperitoneal, laparoscopic, and microsurgical approaches respectively.[33] Sheehan et al. reported 50% and 89% complete pain resolution at 1-month and 1-year post varicocele treatment by embolization.[34]

Conclusions

The principle of varicocele treatment remains unchanged for several decades. Previous reports that showed better outcomes of microsurgical treatment were based on several small studies. Larger studies should be conducted to confirm those advantages. More studies about the technique modification or additional maneuvers to enhance outcomes and reduce complications should also be conducted.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Maheshwari A, Muneer A, Lucky M, Mathur R, McEleny K, British Association of Urological Surgeons and the British Fertility Society. A review of varicocele treatment and fertility outcomes. Hum Fertil Camb Engl 2020;7:1-8.
2. Nagler HM, Luntz RK, Martinis FG. Varicocele. In: Lipshultz LI, Howards SS, editors. Infertility in the Male. 3rd ed. St Louis: Mosbi Year Book; 1997. p. 336-59.
3. Clavijo RI, Carrasquillo R, Ramasamy R. Varicoceles: prevalence and pathogenesis in adult men. Fertil Steril 2017;108:364-9.
4. Schlegel PN, Sigman M, Collura B, De CJ, Eisenberg ML, Lamb DJ, et al. Diagnosis and treatment of infertility in men: AUA/ASRM guideline part I. Male Infertil 2021;115:54-61.
5. Vakalopoulos I, Kampantais S, Lymperi S, Grivas N, Ioannidis A, Mykoniatis I, et al. Should we expand the indications for varicocele treatment? Transl Androl Urol 2017;6:931-42.
6. Al-Said S, Al-Naimi A, Al-Ansari A, Younis N, Shamsodini A, A-sadiq K, et al. Varicocelectomy for male infertility: a comparative study of open, laparoscopic and microsurgical approaches. J Urol 2008;180:266-70.
7. Lee JY, Yu HS, Ham WS, Kang DH, Kim KH, Chung DY, et al. Microsurgical intermediate subinguinal varicocelectomy. Int Surg 2014;99:398-403.

8. Beck EM, Schlegel PN, Goldstein M. Intraoperative varicocele anatomy: A macroscopic and microscopic study. J Urol 1992;148:1190-4.
9. Hopps CV, Lemer ML, Schlegel PN, Goldstein M. intraoperative varicocele anatomy: a microscopic study of the inguinal versus subinguinal approach. J Urol 2003;170:2366-70.
10. Diegidio P, Jhaveri JK, Ghannam S, Pinkhasov R, Shabsigh R, Fisch H. Review of current varicocelectomy techniques and their outcomes. BJU Int 2011; 108:1157-72.
11. Chan P. Management options of varicoceles. Indian J Urol 2011;27:65-73.
12. Al-Kandari AM, Shabaan H, Ibrahim HM, Elshebiny YH, Shokeir AA. Comparison of outcomes of different varicocelectomy techniques: open inguinal, laparoscopic, and subinguinal microscopic varicocelectomy: a randomized clinical trial. Urology 2007;69:417-20.
13. Wu K, Yan G, Yin W, Chen X, Wang G, Cheng Y. A novel approach of microscopic subinguinal varicocelectomy with a "Pulling" Strategy. Urology 2017;104:97-101.
14. Borruto FA, Impellizzeri P, Antonuccio P, Finocchiaro A, Scalfari G, Arena F, et al. Laparoscopic vs open varicocelectomy in children and adolescents: review of the recent literature and meta-analysis. J Pediatr Surg 2010;45:2464-9.
15. Islam S, Paul D, Sarkar S, Islam S, Hanif M. Laparoscopic varicocelectomy by artery preserving and mass ligation technique-a comparative study. J Biomed Eng Med Imaging 2022;9:87-95.
16. Hassan JM, Adams MC, Pope JC 4th, Demarco RT, Brock JW 3rd. Hydrocele formation following laparoscopic varicocelectomy. J Urol 2006;175:1076-9.
17. Rizkala E, Fishman A, Gitlin J, Zelkovic P, Franco I. Long term outcomes of lymphatic sparing laparoscopic varicocelectomy. J Pediatr Urol 2013;9:458-63.
18. Palomo A. Radical cure of varicocele by a new technique; preliminary report. J Urol 1949;61:604-7.
19. Marc G. Surgical management of male infertility. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, editors. Campbell-Walsh Urology. 11th ed. Elsevier: Philadephia; 2016. p. 580-611.
20. Halpern J, Mittal S, Pereira K, Bhatia S, Ramasamy R. Percutaneous embolization of varicocele: technique, indications, relative contraindications, and complications. Asian J Androl 2016;18:234-8.
21. Cassidy D, Jarvi K, Grober E, Lo K. Varicocele surgery or embolization: Which is better? Can Urol Assoc J 2012;6:266-8.
22. Abdulmaaboud MR, Shokeir AA, Farage Y, Abd El-Rahman A, El-Rakhawy MM, Mutabagani H. Treatment of varicocele: a comparative study of conventional open surgery, percutaneous retrograde sclerotherapy, and laparoscopy. Urology 1998; 52:294-300.
23. Çayan S, Shavakhabov S, Kadioğlu A. Treatment of palpable varicocele in infertile men: a meta-analysis to define the best technique. J Androl 2009;30:33-40.
24. Kovac JR, Fantus J, Lipshultz LI, Fischer MA, Klinghoffer Z. Cost-effectiveness analysis reveals microsurgical varicocele repair is superior to percutaneous embolization in the treatment of male infertility. Can Urol Assoc J 2014;8:E619-25.
25. Bebars GA, Zaki A, Dawood AR, El-Gohary MA. Laparoscopic versus open high ligation of the testicular veins for the treatment of varicocele. JSLS 2000;4:209-13.
26. Zampieri N, Zuin V, Corroppolo M, Chironi C, Cervellione RM, Camoglio FS. Varicocele and adolescents: semen quality after 2 different laparoscopic procedures. J Androl 2007;28:727-33.
27. Wang J, Xia SJ, Liu ZH, Tao L, Ge JF, Xu CM, et al. Inguinal and subinguinal micro-varicocelectomy, the optimal surgical management of varicocele: a meta-analysis. Asian J Androl 2015;17:74-80.
28. Wang Q, Liu Y, Wang L. Open, laparoscopic, and microsurgical varicocelectomy for male infertility: a systematic review and meta-analysis. Indian J Surg 2020;82:478-85.
29. Diamond DA, Xuewu J, Cilento Jr BG, Bauer SB, Peters CA, Borer JG, et al. Varicocele surgery: a decade's experience at a children's hospital. BJU Int 2009;104:246-9.
30. Lurvey R, Durbin-Johnson B, Kurzrock EA. Adolescent varicocele: A large multicenter analysis of complications and recurrence in academic programs. J Pediatr Urol 2015 1;11:186.e1-6.
31. Harel M, Herbst KW, Nelson E. Practice patterns in the surgical approach for adolescent varicocelectomy. Springerplus 2015;4:1-6.
32. Al-Gadheeb A, El-Tholoth HS, Albalawi A, Althobity A, AlNumi M, Alafraa T, et al. Microscopic subinguinal varicocelectomy for testicular pain: a retrospective study on outcomes and predictors of pain relief. Basic Clin Androl 2021;31:1.
33. Lundy SD, Sabanegh ES. Varicocele management for infertility and pain: A systematic review. Arab J Urol 2018;16:157-70.
34. Sheehan M, Briody H, O'Neill DC, Bowden D, Davis NF, Given M, et al. Pain relief after varicocele embolization: The patient's perspective. J Med Imaging Radiat Oncol 2020;64:215-9.

Invited Review Article

Retroperitoneal lymph node dissection: the past, present, and future, a review

Shyam Patnaik, John M. Myrga, Robin V. Vasan, Tatum V. Tarin

UPMC Department of Urology, Pittsburgh, PA, USA

Keywords:
Testicular cancer, retroperitoneal lymph node dissection, modified template, nerve-sparing

Abstract

Testicular cancer is a malignancy that impacts young men worldwide. The modern treatment of testicular cancer has evolved due to innovations in medical approaches and surgical techniques. The retroperitoneal lymph node dissection (RPLND) is an integral component in the treatment of testicular cancer. We aim to highlight the advances in surgical approaches and oncologic considerations noted over the past century. Once recognized as a highly morbid procedure, innovations in the understanding of anatomy and minimally invasive approaches have greatly improved patient outcomes. In addition to surgical approaches, we describe oncologic principles associated with modern dissection templates for both non-seminomatous germ cell tumors as well as more recent indications for surgery in seminomatous germ cell tumors. The overall goal of this review is to provide a summary in the utility and recent advances in RPLND techniques.

Insight Urol 2023;44(1):43-50. doi: 10.52786/isu.a.71

Introduction

Testicular cancer is a rare malignancy but remains the most common solid organ malignancy in young men between the ages of 20 to 40 years. The annual rate of new testicular cancer cases was estimated to be 5.9 per 100,000 men in the United States,[1] with incidence rates ranging from ~7 per 100,000 in Europe and Oceania to < 2 per 100,000 men in Asia.[2] Germ cell tumors (GCT) comprise 95% of all testicular malignancies, further being categorized as seminomatous or non-seminomatous germ cell tumor (NSGCT). However, with a multimodal treatment approach including a combination of chemotherapy, radiation, or surgery, 5-year survival rates can be as high as 95%, regardless of stage.[3]

When staging testicular cancer, computed tomography (CT) imaging has improved diagnosis of extragonadal spread. However, even with advances in CT imaging, up to 20-30% of patients can be understaged based on the size cutoffs used for lymphadenopathy (typically 1 cm in the short axis).[4] GCT has a predictable pattern of metastasis which follows lymph drainage, with right-sided tumors initially metastasizing to the nodes between the aorta and the inferior vena cava (interaortocaval nodes) and left-sided tumors initially spreading to the nodes lateral to the aorta (para-aortic).[5,6] Retroperitoneal lymph node dissection (RPLND) is an important

Corresponding author: Shyam Patnaik
Address: 3471 Fifth Ave Suite 700, Pittsburgh, PA 15213, USA
E-mail: patnaiks2@upmc.edu
Manuscript received: April 24, 2023
Revision received: May 25, 2023
Accepted after revision: June 2, 2023

surgical procedure for diagnosis and treatment of extra-testicular disease.

In this review, we will discuss the evolution of techniques for RPLND in its role for management in testicular cancer over time.

Historical Technique

Dr. Most in 1898 was one of the first surgeons to note the extragonadal lymphatic spread of testicular cancer up to the paraaortic nodes near the renal hilum.[7] Surgeons then began performing techniques to treat these extragonadal metastasis. Some of the earliest reports of the RPLND were described by Frank Hinman in 1914.[8] He described RPLND being performed in France, England, and Italy between 1905 and 1914. His description of the technique involved a two-step procedure, starting with an inguinal incision for the radical orchiectomy and then extending the inguinal incision superiorly up towards the flank.

In the middle of the 20th century, mainly after World War II, there was an increasing number of patients treated with transabdominal RPLND after orchiectomy.[9] Around 1950, it was noted that unilateral RPLND was insufficient in up to one third of cases, leading to implementation of a bilateral template. In 1985, Farley et al. described their series of 98 patients who underwent extended supra-hilar RPLND through a midline incision.[10] Interestingly, they excised the renal fascia, perirenal fat, and adrenal gland on the side of the tumor. They performed unilateral dissection down to the bifurcation of the common iliac vessels. Reported complications from their study included ileus (most common), pleural effusion, and pneumonia. In terms of oncologic outcome, 16% of the 57 patients who had RPLND for stage I testicular cancer had relapse between 5-11 months after surgery requiring chemotherapy.[10]

The technique of the RPLND continued to evolve as surgeons turned their attention to variations in the surgical template. Donahue et al. described the evolution of their RPLND technique from 1965 to 1989 for stage 1 testicular cancer.[11] Their study highlighted the progression of their technique starting with the traditional bilateral supra-hilar extended RPLND to the bilateral infra-hilar RPLND and then to a modified unilateral RPLND in an attempt to preserve ejaculatory function. Almost 75% of patients who had modified unilateral template RPLND had preserved ejaculation. This prompted further investigation into prospective nerve-sparing by pre-dissection identification of the lumbar postganglionic nerves and preservation of these nerve trunks to improve ejaculation outcomes. With this modification in technique, nerve-sparing (NS) modified template RPLND led to 98% preserved ejaculation.[11] There was no significant difference in relapse rate between supra-hilar, bilateral infra-hilar, and modified unilateral templates for these patients, with around 11% of patients with stage 1 disease having relapse for each template.

As the RPLND has developed, it has evolved to serve multiple roles. The RPLND serves a diagnostic role by providing pathology to allow for confirmation of staging as well as performing a therapeutic role in removal of disease. It can potentially cure patients with N1 nodal disease with surgery alone, thereby avoiding chemotherapy.[12] Additionally, if chemotherapy was primary treatment, RPLND can be performed to remove residual disease.[12]

Full Bilateral Template RPLND

With the development of the RPLND over time, the variations in technique led to the development of the full bilateral template RPLND for oncologic control (Table 1). In a retrospective study of 283 patients who underwent RPLND, the retroperitoneal spread of primary testicular cancer was shown to vary between right and left primary testicular tumors.[5] Right-sided testicular tumors spread to the ipsilateral retroperitoneal lymph nodes 85% of the time, with 13% to ipsilateral and contralateral lymph nodes and finally only to the contralateral side in ~2%.[5] Left-sided testicular tumors had extragonadal spread to the ipsilateral retroperitoneum 80% of the time, with 20% in bilateral retroperitoneal lymph nodes.[5] As such, the standard full template RPLND involves dissection of the retroperitoneal lymph nodes between the following landmarks: renal vessels superiorly, ureters laterally, and the iliac vessels inferiorly.[13] Use of the 'split-and-roll' technique allows for careful dissection of lymph node tissue over the IVC and aorta. The technique involves splitting the lymphatics on the plane over the adventitia of the great vessels and rolling them to identify other branches of the vessels.[13] The RPLND is performed most commonly through a large midline incision with a transperitoneal

Table 1. Summary of studies over the development of the RPLND

Highlighted Papers	Number of Patients	Key Findings
Anatomy and Templates		
Ray et al. – 1973	283	Lymphatic drainage from testicles follows predictable patterns which set the stage for modern templates
Fraley et al. – 1985	98	Suprahilar bilateral template RPLND with chemo led to survival rates of 88% in stage II disease and 100% survival in stage I disease.
Donohoe et al. – 1993	464	Evolution from the bilateral suprahilar to infrahilar bilateral template with nerve sparing and introduction of unilateral template over 25 years with comparable rates of relapse. Ejaculation preserved in 98% of patients.
Extraperitoneal		
Kim et al. – 2012	12	Extraperitoneal approach had greater lymph node yield, shorter operative times, lower blood loss, and shorter length of stay
Syan-Bhanvadia et al. – 2017	69	The approach was safely used in post-chemotherapy patients and confirmed prior results. 5.7 retroperitoneal relapse rate
Robotic Assisted		
Pearce et al. – 2017	47	Primary RPLND. 96% had modified unilateral template. Median OR time 235min, blood loss 50 mL, post-op length of stay 1 day. 2-year recurrence-free survival rate of 97%. Median of 26 nodes per patient.
Rocco et al. – 2020	58	Primary RPLND alone. Bilateral and unilateral templates used. Median OR times of 319 minutes, blood loss of 100 mL, and post-op length of stay of 2 days. 2 year recurrence-free survival rate of 91%. Median of 26 nodes per patient.
Ohlmann et al. – 2021	23	Bilateral and unilateral templates were feasible with appropriate lymph node yield. Approach can be utilized with primary and post-chemo patients. No recurrence at 16-month follow-up
Prospective Trials in Seminoma		
Daneshmand et al. – 2023	55	SEMS Trial. Stage I relapse or newly diagnosed stage II disease (Lymph nodes between 1-3cm, 2 maximum). 81 % recurrence-free survival at 2 years. 13% complication rate. 3 patients had long term anejaculation (all 3 did not have nerve sparing).
Hiester et al. – 2022	33	PRIMETEST Trial. Stage I relapse or newly diagnosed staged II disease (lymph nodes less than 5cm, no maximum). Unilateral template. Study showed progression-free survival of 70%. Did not meet endpoints and could not recommend primary RPLND for seminoma outside of clinical trial at this time
Heidenreich et al. – 2023	16	COTRIMS Trial. Stage II disease. Open or robotic approach. Varied template. Showed 8% recurrence-free survival. Salvaged with chemotherapy. No long-term complications noted.

approach. In a retrospective review of 157 patients who had full template bilateral primary RPLND for low-stage NSGCT, median total lymph node yield was 28 lymph nodes.[14] This study suggested that higher lymph node yield was associated with lower risk of relapse, with mean 5-year recurrence-free survival of 91% vs 79% for yields ≥ 28 vs < 28 nodes respectively.

Complications of RPLND include ileus, small bowel obstruction (SBO), venous thromboembolism (VTE), chylous ascites, and ejaculatory dysfunction.[15] Ejaculatory dysfunction is a result of injury to the sympathetic nerves of the hypogastric plexus and lumbar post-ganglionic sympathetic fibers (especially L2-L4) since these nerves stimulate antegrade ejaculation.[16] In an effort

to improve nerve-sparing to reduce ejaculatory dysfunction, modified templates were developed since preservation of the ipsilateral sympathetic nerve trunks below the inferior mesenteric artery (IMA) was seen to improve antegrade ejaculation.

Modified Unilateral Template RPLND

Right

In patients with disease limited to right side on imaging, RPLND was performed with the following landmarks: right renal vessels superiorly, right ureter laterally, periaortic lymphatic above the IMA medially, and the right iliac vessels inferiorly.[13] The nodes resected include paracaval, precaval, interaortocaval, and preaortic lymph nodes.[13,17] The iliac nodes and ipsilateral gonadal vein are also removed.

Left

The left modified unilateral template RPLND involves dissection of lymph nodes between the following landmarks: left renal vessels superiorly, left ureter laterally, periaortic lymphatic above the inferior mesenteric artery (IMA) medially, and the left iliac vessels inferiorly.[13] The nodes resected in this template include the paraaortic, preaortic, interaortocaval lymph nodes.[17] The iliac nodes and ipsilateral gonadal vein are also removed.

Oncologic outcomes

However, as modified unilateral templates have evolved, their oncologic outcomes have been a key point of interest. Eggener et al. showed that the risk of disease outside of the modified unilateral templates ranged between 3 to 23% for patients with stage II testicular cancer.[18] They studied 5 modified templates, 3 of which were open (Testicular Tumor Study Group (TTSG), Memorial Sloan-Kettering Cancer Center (MSKCC), and Indiana University), and 2 laparoscopic templates (The Johns Hopkins University and the University of Innsbruck). While extra-template disease was as high as 23%, they highlighted that if the right-sided dissection templates included preaortic, paraaortic and right common iliac nodes, residual disease outside of the right side template came down to 2%. For left template RPLND, inclusion of interaortocaval, precaval, paracaval and left common iliac nodes could lead to only 3% of missed extra-template disease.[18] The main point was that inclusion of these lymph nodes in the bilateral infrahilar full template RPLND with nerve-sparing allowed for the best oncologic outcomes while still preserving fertility.

In a recent study of 274 patients, 94% of whom had RPLND using a modified unilateral template, there was no difference in recurrence-free survival between modified and bilateral template.[19] They described their left modified technique as dissection of the preaortic, paraaortic, retro-aortic and left common iliac lymph nodes and their right modified template included dissection of the preaortic, interaortocaval, retro-aortic, paracaval, retrocaval and right common iliac nodes. This study included 126 patients with pathologic stage II disease (46%). The use of primary RPLND for treatment of stage II NSGCT led to 81% who were cured through surgery alone. In 55 months after RPLND, 12% of patients had recurrence. Of these 33 recurrences, only 1.6% of these recurrences occurred in the contralateral retroperitoneum. There was concern that 4 out of the 7 relapses were extra-template, which could be avoided with a full template bilateral nerve-sparing RPLND while still preserving fertility.[20] Overall survival for the entire patient group was 98% regardless of surgical templates.

The use of modified unilateral templates is still debated, especially considering the fact that use of full bilateral template with nerve-sparing can achieve good rates of antegrade ejaculation without compromising on oncologic outcomes. With the risk of residual extra-template disease with use of modified unilateral templates, there is risk of late relapse, need for re-operative RPLND and the need for additional chemotherapy.[18] Importantly, the most common pathology during a repeat procedure is teratoma, which is resistant to both chemotherapy and radiotherapy.[21] Repeat RPLND increases the risks of surgical complications, which can be as high as 30% in the perioperative period.[21] Additionally, the long term risks of chemotherapy are becoming increasingly evident, including risk of secondary malignancy, cardiovascular dysfunction, and impaired mental function.[22] As such, use of modified unilateral templates is an area that is still being studied and remains controversial.

Extraperitoneal RPLND

Another modification to the standard transabdominal RPLND technique is the development

of the extraperitoneal RPLND. The rationale for this technique arose from an attempt to reduce gastrointestinal complications such as ileus or small bowel obstruction as well as inadvertent bowel injury. A study in 2012 evaluated clinical outcomes of a single surgeon experience with 12 patients who underwent midline extraperitoneal RPLND compared to transperitoneal RPLND.[23] In this small series of patients, the extraperitoneal approach had decreased blood loss (mean 305mL vs 517mL for transperitoneal), shorter operative time (292 min vs 334 min for transperitoneal) and greater lymph node yield (44 vs 29 lymph nodes for transperitoneal).[23] They also showed statistically significant shorter return of bowel function (1.7 days vs 2.9 days for transperitoneal) and shorter length of stay (3.3 days vs 5.3 days for transperitoneal).[23] Their described technique starts with a midline abdominal incision from xiphoid to just cephalad to the pubic symphysis. Careful blunt dissection was performed to keep the peritoneum intact and then sweep the peritoneal contents medially. The authors emphasized caution with dissecting off the anterior peritoneum due to its relative thinness. The dissection of the peritoneum was continued until the peritoneum was mobilized up to the contralateral renal hilum. The remainder of the lymph node dissection was then performed in the standard fashion. The authors reported no evidence of retroperitoneal recurrence at a median follow-up time of 196 days. This presentation of technique was however, limited by small sample size and limited follow-up period.

In 2017, this group expanded on their initial series to evaluate 69 patients who underwent extraperitoneal RPLND between 2010 and 2015.[24] Primary extraperitoneal RPLND had extended ipsilateral templates for resection and their post-chemotherapy resections underwent full bilateral template vs extended ipsilateral templates. In the overall cohort, 1 out of 69 patients required conversion to the transperitoneal approach due to inability to progress through the case. Of the remaining 68 patients who successfully had extraperitoneal RPLND, primary RPLND was performed in 27 patients and 41 had post-chemotherapy RPLND. They showed a median length of stay of 3 days postoperatively and median of two days for return of bowel function.[24] They had a median yield of 36 nodes for their extraperitoneal approach. In this series, 4 patients had retroperitoneal relapse, with one patient having relapse after post-chemotherapy RPLND. These patients had successful salvage treatment with chemotherapy and the authors felt that oncologic outcomes were not compromised with the extraperitoneal approach.

Minimally Invasive Techniques

Robotic-assisted laparoscopic RPLND

Robot-assisted laparoscopic RPLND was developed an effort to improve on the laparoscopic technique. Robotic RPLND has been mainly utilized in low clinical stage, low volume disease. While multiple studies have shown that factors such as blood loss, length of stay, and visualization are improved with robot-assisted RPLND,[25,26] there is still debate of this technique regarding oncologic outcomes. In a study of 23 patients who had robotic RPLND, with a mix of primary and post-chemotherapy RPLND (7 vs 16 respectively), median lymph node yield was 11 nodes.[27] When stratified by bilateral template, lymph node yield was 26 nodes compared to 12 nodes for modified unilateral template. At a median follow up time of 16 months, this study reported no recurrence or death.

In a multicenter institution series, Pearce et al. studied the outcomes of 47 patients who had primary robotic RPLND for low-stage NSGCT between 2011 and 2014.28 Modified unilateral template was used in 96% of patients, with nerve-sparing performed per surgeon discretion. There was a median lymph node yield of 26 nodes per patient. Eight patients had node positive disease on RPLND, with 5 receiving adjuvant chemotherapy.28 Their reported 2-year recurrence-free survival rate was 97%, however their median follow-up time was 16 months. One patient had conversion to open procedure due to aortic injury but overall complication rate was found to be 9% for early complications (< 30 days; chyle leak, ileus) and 0% for late complications. All patients had preserved antegrade ejaculation. The authors concluded that robotic RPLND has promising early oncologic outcomes and complication rates but long-term data was required to truly evaluate its use as a therapeutic procedure.

Rocco et al. studied the outcomes of primary robotic RPLND in low stage disease. In their 58 patients, performed between 2008-2019, they had

a 2-year recurrence-free survival rate of 91%.[29] Of note, the authors did initially use a modified unilateral template, but overall, 69% of their patients had full bilateral template dissection. In terms of the logistics of their robotic technique, their median operative time was 319 minutes, median blood loss was 100 mL, and they had a median yield of 26 nodes per case.[29] Their patients stayed for a median of 2 days after surgery. The use of a retroperitoneal 'hammock' is described in multiple studies as a method to secure the peritoneum to the abdominal wall.[29–31]

Based on these studies, robotic RPLND is still to be considered in select patients but should be performed by experienced surgeons. As more long-term data is acquired on surgical and oncologic outcomes from robotic RPLND, the implementation of robotic RPLND may increase, especially as robotic techniques improve as well.

Primary RPLND for Seminoma

One area of increased interest is the use of RPLND as a primary mode of treatment for patients with seminoma. For stage I seminomas, EUA and AUA guidelines suggest the use of surveillance or chemotherapy, while management of stage II seminoma consists of chemotherapy or radiation.[32] RPLND has primarily been reserved in the post-chemotherapy setting for FDG-avid lesions.[32] While highly effective, these treatments are often associated with significant long-term cardiopulmonary, renal, and reproductive consequences from chemotherapy.[22] Recent prospective studies in stage II seminoma have shown utility in the use of RPLND for primary disease management.

The Surgery in Early Metastatic Seminoma (SEMS) trial looked at 55 patients across 12 sites between USA and Canada with isolated stage 1 relapse between 1-3 cm or newly diagnosed stage II disease with no more than two 1-3 cm lymph nodes on staging imaging.[33] These individuals underwent modified ipsilateral template or bilateral template RPLND per surgeon discretion (35% had bilateral RPLND). Extraperitoneal approach was utilized in 27% of patients had RPLND. Of the total cohort, 87% of their patients had nerve-sparing, with overall 5% of patients having anejaculation (notably in patients who did not have nerve-sparing). With a median follow-up time of 33 months, the 2-year recurrence-free survival was noted to be 81%. Overall survival was noted to be 100% at 24 months. In the 12 patients who had a recurrence of disease, 75% had chemotherapy and 25% underwent additional surgery.

Another prospective trial, the PRIMETEST trial, examined outcomes of primary RPLND in 33 patients with stage I disease with relapse, or stage IIA/B disease with lymph nodes up to 5cm in size.[34] Compared to the SEMS trial, this study examined only unilateral templates (42% were open, 58% robotic approach). Their study showed 10 recurrences (30%), with progression free survival of 70%, 7 of which were outside of their operative field at their 32 month follow-up timeline.[34] Their study did not meet their primary endpoint of a recurrence rate less than 30%. However, they concluded that surgery with a unilateral template shows promise in highly selected patients but could not be recommended at this time outside of further clinical evaluations.[34]

The COTRIMS trial is a prospective clinical trial where primary nerve sparing RPLND was performed on 16 patients with stage II seminoma, where clinical stage was IIA (13 patients) or IIB (3 patients).[35] Open nerve-sparing RPLND was performed in 14 patients, with 2 of 16 having robotic-assisted procedures. Ejaculation was preserved in almost 88% of the cohort and the study noted no high grade surgical complications (greater than Clavien-Dindo grade 3A). Relapse was found on 4 and 6 month follow up out-of-field in 2 of 16 patients (12.5%), which was salvaged with chemotherapy.[35] While limited in sample size and long term follow-up, these trials suggest that nerve-sparing RPLND can be performed as a primary treatment in an effort to reduce treatment morbidity from chemotherapy or radiation with relatively low complication rate in the hands of experienced surgeons.

Conclusion

RPLND is a diagnostic and therapeutic procedure that is continuing to evolve to improve patient outcomes from testicular cancer. Oncologic outcomes should be prioritized when determining template selection and technique for performing RPLND. Advances in techniques such as open extraperitoneal RPLND, nerve-sparing, and development of robotic-assisted laparoscopic RPLND have aimed to reduce surgical complication, preserve antegrade ejaculation, and maintain

oncologic outcomes. A new promising area of study is the use of primary RPLND for treatment in select patients with low stage seminoma, with the goal of limiting the side effects of chemotherapy and radiation in this young patient population. The indications for RPLND continue to expand, as it remains an integral component of the multimodal management of testicular cancer.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Cancer of the Testis - Cancer Stat Facts. NIH SEER [Internet]. [cited 2023 February 22]. Available from: https://seer.cancer.gov/statfacts/html/testis.html
2. Znaor A, Skakkebaek NE, Rajpert-De Meyts E, Kuliš T, Laversanne M, Gurney J, et al. Global patterns in testicular cancer incidence and mortality in 2020. Int J Cancer 2022;151:692-8.
3. Fung C, Dinh PC, Fossa SD, Travis LB. Testicular cancer survivorship. J Natl Compr Cancer Netw JNCCN 2019;17:1557-68.
4. Leibovitch L, Foster RS, Kopecky KK, Donohue JP. Improved accuracy of computerized tomography based clinical staging in low stage nonseminomatous germ cell cancer using size criteria of retroperitoneal lymph nodes. J Urol 1995;154:1759-63.
5. Ray B, Hajdu SI, Whitmore Jr WF. Distribution of retroperitoneal lymph node metastases in testicular germinal tumors. Cancer 1974;33:340-8.
6. Donohue JP, Zachary JM, Maynard BR. Distribution of nodal metastases in nonseminomatous testis cancer. J Urol 1982;128:315-20.
7. Hendry WF. Retroperitoneal lymphadenectomy in the management of testis cancer. In: Neal DE, editor. Tumours in urology. Springer: London; 1994. p. 273-92.
8. Hinman F. The operative treatment of tumors of the testicle: with the report of thirty cases treated by orchidectomy. J Am Med Assoc 1914;LXIII:2009-15.
9. Donohue JP. Evolution of retroperitoneal lymphadenectomy (RPLND) in the management of non-seminomatous testicular cancer (NSGCT). Urol Oncol 2003;21:129-32.
10. Fraley EE, Narayan P, Vogelzang NJ, Kennedy BJ, Lange PH. Surgical treatment of patients with stages I and II nonseminomatous testicular cancer. J Urol 1985;134:70-3.
11. Donohue JP, Thornhill JA, Foster RS, Rowland RG, Bihrle R. Retroperitoneal lymphadenectomy for clinical stage A testis cancer (1965 to 1989): modifications of technique and impact on ejaculation. J Urol 1993;149:237-23.
12. Krege S, Rübben H. [Lymphadenectomy for testicular cancer. Diagnostic and prognostic significance as well as therapeutic benefit]. Urol Ausg A 2005;44:652-6.
13. Tran V, Gibson L, Sengupta S. Retroperitoneal lymph node dissection for germ cell tumour. Transl Androl Urol 2020;9:3103-11.
14. Nayan M, Jewett MAS, Sweet J, Anson-Cartwright L, Bedard PL, Moore M, et al. Lymph node yield in primary retroperitoneal lymph node dissection for nonseminoma germ cell tumors. J Urol 2015;194: 386-91.
15. Subramanian VS, Nguyen CT, Stephenson AJ, Klein EA. Complications of open primary and post-chemotherapy retroperitoneal lymph node dissection for testicular cancer. Urol Oncol 2010;28:504-9.
16. Jewett MAS, Groll RJ. Nerve-sparing retroperitoneal lymphadenectomy. Urol Clin North Am 2007;34: 149-58.
17. Tanaka T, Kitamura H, Kunishima Y, Takahashi S, Takahashi A, Masumori N, et al. Modified and bilateral retroperitoneal lymph node dissection for testicular cancer: peri- and postoperative complications and therapeutic outcome. Jpn J Clin Oncol 2006;36:381-6.
18. Eggener SE, Carver BS, Sharp DS, Motzer RJ, Bosl GJ, Sheinfeld J. Incidence of disease outside modified retroperitoneal lymph node dissection templates in clinical stage I or IIA nonseminomatous germ cell testicular cancer. J Urol 2007;177:937-42; discussion 942-43.
19. Douglawi A, Calaway A, Tachibana I, Barboza MP, Speir R, Masterson T, et al. Long-term oncologic outcomes after primary retroperitoneal lymph node dissection: minimizing the need for adjuvant chemotherapy. J Urol 2020;204:96-103.
20. Sheinfeld J, DiNatale RG, Carver B. Editorial comment. J Urol 2020;204:101-2.
21. McKiernan JM, Motzer RJ, Bajorin DF, Bacik J, Bosl GJ, Sheinfeld J. Reoperative retroperitoneal surgery for nonseminomatous germ cell tumor: clinical presentation, patterns of recurrence, and outcome. Urology 2003;62:732-6.
22. Fung C, Dinh P, Ardeshir-Rouhani-Fard S, Schaffer K, Fossa SD, Travis LB. Toxicities associated with cisplatin-based chemotherapy and radiotherapy in long-term testicular cancer survivors. Adv Urol 2018;2018:e8671832.
23. Kim P, Syan-Bhanvadia S, Djaladat H, Faber K, Tadros NN, Nichols C, et al. Midline extraperitoneal approach for retroperitoneal lymph node dissection for testicular germ cell tumor. Urology 2012;80:941-5.
24. Syan-Bhanvadia S, Bazargani ST, Clifford TG, Cai J,

Miranda G, Daneshmand S. Midline extraperitoneal approach to retroperitoneal lymph node dissection in testicular cancer: minimizing surgical morbidity. Eur Urol 2017;72:814-20.
25. Davol P, Sumfest J, Rukstalis D. Robotic-assisted laparoscopic retroperitoneal lymph node dissection. Urology 2006;67:199.
26. Williams SB, Lau CS, Josephson DY. Initial series of robot-assisted laparoscopic retroperitoneal lymph node dissection for clinical stage I nonseminomatous germ cell testicular cancer. Eur Urol 2011;60: 1299-302.
27. Ohlmann CH, Saar M, Pierchalla LC, Zangana M, Bonaventura A, Stöckle M, et al. Indications, feasibility and outcome of robotic retroperitoneal lymph node dissection for metastatic testicular germ cell tumours. Sci Rep 2021;11:10700.
28. Pearce SM, Golan S, Gorin MA, Luckenbaugh AN, Williams SB, Ward JF, et al. Safety and early oncologic effectiveness of primary robotic retroperitoneal lymph node dissection for nonseminomatous germ cell testicular cancer. Eur Urol 2017;71:476-82.
29. Rocco NR, Stroup SP, Abdul-Muhsin HM, Marshall MT, Santomauro M, Christman MS, et al. Primary robotic RLPND for nonseminomatous germ cell testicular cancer: a two-center analysis of intermediate oncologic and safety outcomes. World J Urol 2020;38:859-67.
30. Mittakanti HR, Porter JR. Robot-assisted laparoscopic retroperitoneal lymph node dissection: a minimally invasive surgical approach for testicular cancer. Transl Androl Urol 2020;9:S66-73.
31. Santomauro MG, Stroup SP, L'Esperance AH, Masterson JH, Derweesh IH, Auge BK, et al. Supine robotic-assisted retroperitoneal lymph node dissection for testicular cancer. CRSLS e2014.00326.
32. Stephenson A, Eggener SE, Bass EB, Chelnick M, Daneshmand S, Feldman D, et al. Diagnosis and treatment of early stage testicular cancer: AUA Guideline. J Urol 2019;202:272-81.
33. Daneshmand S, Cary C, Masterson T, Einhorn L, Adra N, Boorjian SA, et al. Surgery in early metastatic seminoma: a phase II trial of retroperitoneal lymph node dissection for testicular seminoma with limited retroperitoneal lymphadenopathy. J Clin Oncol Off J Am Soc Clin Oncol 2023;41:3009-18.
34. Hiester A, Che Y, Lusch A, Kuß O, Niegisch G, Lorch A, et al. Phase 2 single-arm trial of primary retroperitoneal lymph node dissection in patients with seminomatous testicular germ cell tumors with clinical stage IIA/B (PRIMETEST). Eur Urol 2022;S0302-2838(22)02775-0.
35. Heidenreich A, Paffenholz P, Nestler T, Pfister DA. Nerve sparing retroperitoneal lymph node dissection in clinical stage IIA/B seminoma: The COTRIMS trial. J Clin Oncol 2022;40:418.

Instructions for Authors

The Insight Urology (ISU) is the official journal of the Thai Urological Association under the Royal Patronage (TUA). The Editorial Board welcomes all scientific manuscripts from physicians and various specialties which are of interest and of benefit to the urological society. The submitted manuscripts must not be in the process of submission or have been previously published in any other journal.

Types of manuscripts

1. Original article

Requirements:

1.1 Abstract
- Objective (s)
- Materials and Methods
- Results
- Conclusion (s)

1.2 Full text
- Introduction
- Objective (s)
- Materials and Methods
- Results
- Discussion
- Conclusion (s)
- Acknowledgement (optional)
- Conflict of Interest
- References

1.3 Table (s) and legend (s)

1.4 Figure (s) and legend (s)

2. Review article

Requirements:

2.1 Interesting and pertinent

2.2 Include standard of treatment

3. Case report

Requirements:

3.1 Interesting

3.2 Not previously published

3.3 Indicates the important case aspects

4. Letter to the editor

Requirements:

4.1 Questions, discussions, and opinions to published articles

4.2 Creative and beneficial to all readers

4.3 Negative opinions must include reference (s) for the opposing opinion

5. Surgical technique

Requirements:

5.1 Reports of surgical technique

5.2 The technique provides beneficial to readers

5.3 The technique has positive treatment results after surgeries

Manuscript preparation

The Insight Urology will be maintained according to the international standards set by the International Committee of Medical Journal Editors for the conduct, reporting, editing and publication of scholarly work in medical journals.

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:
   - Type of article
   - Title
   - Authors' names, titles, degrees, and academic positions
   - Authors' affiliations
   - Corresponding author's address, including email address, telephone number and fax number
   - Number of pages of the manuscript, references, tables, and figures (OR-You could say, "Length of manuscript, including text, references, tables and figures")

References guideline

The authors must use Vancouver style and use Arabic numbers as seen in the manuscript. Use superscript numbers in-text to cite sources of information. Superscript numbers are in order of citation. The superscript number is inserted

into the document immediately next to the fact, concept, or quotation being cited. If citing more than one reference at the same point, separate the numbers with commas and no spaces between. The short name of the journal must follow Index Medicus format.

Examples for references

1. English article: List all authors' names if less than seven. If seven or more authors, list only the first six names and follow by et al.

For example:

- Kalantar-Zadeh K, Li P, Tantisattamo E, Kumaraswami L, Liakopoulos V, Lui, S, et al. Living well with kidney disease by patient and care-partner empowerment: kidney health for everyone everywhere. Insight Urol 2021;42:69-78.

If the authors are committees, groups, or institutes:

- Report of the International Reflux Study Committee. Medical versus surgical treatment of primary vesicoureteral reflux. Pediatrics 1981;67:392-400.

2. Thai articles must be translated to English language. Dates must be changed to the Gregorian calendar if originally listed in Buddhist calendar format. Use the same reference pattern as for English articles.

3. If the reference is a reference from a total book cite it as follows:

- Author (s) or editor (s) name. Book's name. Edition. City of publishing: Publisher; Year of publication.
- Mostofi JFR, Sesterhennl A, Sobin LH. International Histological Classification of Prostate Tumours. Geneva: WHO; 1980.

4. If the reference is a reference from a book chapter cite it as follows:

- Author (s) name. Name of book chapter. In: editor (s) name, editor (s). Book's name. Edition. City of publishing: Publisher; Year of publication: Page.
- Barry JM, Colin MJ, Renal transplantation. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, editors. Campbell-Walsh Urology. 10th ed. Philadelphia: Elsevier Saunders; 2012. p. 1126-53.

Table

1. Each table should be placed on a separate page. One page for one table.
2. All tables should have the table number with table description on the top of the table.
3. Additional explanations should put *, ¥, etc., in the table and then give more detail on the bottom of the table.
4. Every table must be referenced in the article.

Figure

1. Hand-drawn figures must be drawn with thick, black lines.
2. Photos can be black and white or color. Use arrows to indicate important parts of the picture. All figures must have legends.
3. Patients must not be identifiable from any part of any photo.

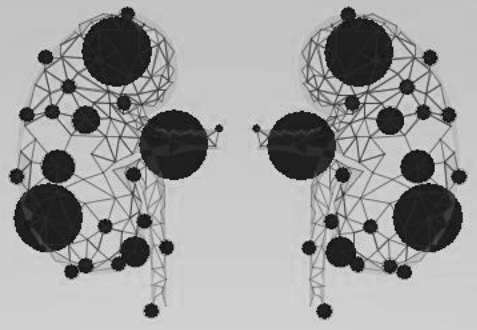
Abbreviation and measurement

1. Use standard abbreviations. Should not use abbreviation in the Title or Abstract. All abbreviations must be first typed in entirety with the abbreviation in parentheses/braces before continued use in abbreviated form.
2. Use metric units for length, height, weight, and volume (meter, kilogram, and litter), with only 2-decimal accuracy.
3. Use degree Celsius for temperature.
4. Use International System of Unit (SI) for all laboratory and chemical results.

Submission of manuscript

Online submission:
www.tci-thaijo.org/index.php/TJU/about/submissions

Insight UROLOGY



The Thai Urological Association under the Royal Patronage

7th Floor, Royal Golden Jubilee Building, 2 Soi Soonvijai, New Petchaburi Road, Bangkapi, Huaykwang, Bangkok 10310, Thailand

www.tuanet.org