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Safety and efficacy of thermo-expandable metallic stent in ureteral stricture following gynecological malignancy surgery and radiotherapy: a single center experience with 33 cases

Yuyu Xu[1†], Zhiduan Cai[1†], Shuangxing Chen[1†], Qingling Xie[1], Zewen Zhou[1], Haishan Zhuang[1], Ning Liang[3], Jiaywei Tsauo[4*] and Guibin Xu[1,2*]

Abstract

Background The effectiveness of metallic stents in treating ureteral strictures following surgery and radiotherapy for gynecological tumors is currently uncertain. We aimed to investigate the efficacy and safety of thermo-expandable metallic stent (Memokath) in the treatment of ureteral stricture after radiotherapy for gynecological tumors.

Methods In this descriptive cross-sectional study, 27 patients with ureteral stricture were treated with Memokath stent after gynecological tumor radiotherapy with or without chemotherapy that was admitted to our hospital from August 2021 to August 2023. Clinical data on efficacy, safety, and complications during stent insertion and indwelling were analyzed.

Results The successful insertion of thirty-three stents in twenty-seven patients studied. The stenosis length was 10.14 ± 6.76 cm, and the hospitalization was 4.43 ± 1.83 days. One patient has died from the primary disease carrying a patency stent. The Kaplan-Meier graph showed that the cumilative patency rate of patients with thermo-expandable metallic stent were 92.4% (SD = 5.2%) in eight months, 77.4% (9.1%) in 12 months and 67.7% (SD = 12%) in 29 months, while the cumilative survival rate was 87.5% (SD = 11.5%) in 29 months. The stent patency was 81.48% and later complications of stent indwelling were 5/27, including refractory urinary tract infection (UTI) in three cases, stent migration, and stent intolerance respectively. The creatinine levels, hydronephrosis degree, and glomerular filtration rate improved after the operation, and the first two indicators were statistically significant.

†Yuyu Xu, Zhiduan Cai and Shuangxing Chen contributed equally to this work.

*Correspondence:
Jiaywei Tsauo
80732059@qq.com
Guibin Xu
uro_xgb@163.com

Full list of author information is available at the end of the article

Conclusion Memokath stent is a safe and effective treatment for ureteral stricture after surgery and radiotherapy with or without chemotherapy for gynecological tumors.

Keywords Ureteral stricture, Radiotherapy, Thermo-expandable metallic stent, Real-world study, Efficacy analysis

Introduction

Radiation therapy (RT) is the most important means to control gynecological tumors. Nevertheless, ureteral stricture after RT for gynecological tumors has become particularly prominent. As a late complication of radiotherapy, it can lead to hypronedrosis and impair renal function, causing from narrowing flow of urine from the kidney to the bladder. Endourological approaches offer minimally invasive options with potentially less morbidity. However, frequent exchanges of double-J stents or nephrostomy tubes have been related to increased medical costs and the reduced quality of life [1, 2]. Moreover, this kind of ureteral stenosis is characterized by time progression and tissue fibrosis, so it is prone to be occlusion because of extrinsic compression [3].

Memokath 051 stent (PNN Medical, Copenhagen, Denmark) has recently been shown to be an attractive long-term and cost-effective minimally invasive option for both benign and malignant ureteral strictures [4–8]. At present, there are still few studies to analyze the safety and efficacy of Memokath stent in ureteral stricture after RT for gynecological tumors. Therefore, we presented our study of the Memokath stent in the treatment of stricture following surgery and/or radiotherapy for gynecological tumor.

Patients and methods

Ethical standards

Our study received approval from our institution's Ethics Committee (GYWY-L2024-03, January 17th, 2024), and the need for patient consent was waived due to its retrospective nature.

Study design

We searched the hospital's inpatient system to identify patients with US post-RT for gynecological tumors, treated with Memokath from August 2021 to August 2023. We included all identified patients in the study without exclusions. We collated and analyzed patient demographics and clinical characteristics, procedure details, and follow-up data. The primary outcome measure was the Memokath stent's patency rate, with complications and GFR as secondary outcomes. The ureter can be radiographically divided into three parts: proximal ureter: from the renal pelvis to the pelvic brim; middle ureter: from the pelvic brim to the bladder; distal ureter: within the bladder wall. Stent patency was defined as the stent remaining in situ without migration or causing progressive ureteral obstruction (increased hydronephrosis). Stent intolerance is defined as without urinary tract infection or stent obstruction, the repeated or progressive aggravation of discomfort was caused by the stent, especially inconvenience and unpleasantness to the patient's life. Hydronephrosis volume, measured by ultrasonography, was calculated as length x width x depth x 0.523 [9]. Glomerular filtration rate (GFR) assessment was performed using single-photon emission computed tomography (SPECT). We graded complications using the Clavien-Dindo classification [10]. Cost analysis included both stent and anesthesia expenses. Operative time spanned from ureteroscope insertion to stent placement completion. Length of hospital stay was the duration from surgery to discharge.

Surgical procedure

All surgical treatment were performed with no abnormal urinalysis or negative urine culture. A part of patients with refractory urinary tract infection or pyonephrosis, would be performed with a percutaneous nephrostomy catheter. All operations were performed by the same surgeon. Under spinal anesthesia, retrograde urography was used to record and measure the location and degree of the US (Fig. 1A). A length-measuring catheter was inserted to determine the stenosis length, aiding in proper stent selection (Fig. 1B). Under fluoroscopic guidance, a guidewire was inserted into the renal pelvis. The Memokath outer sheath device was then inserted over the previously placed guidewire to cover the stricture segment. If the device could not pass through, an F15 balloon dilator was used to expand the stricture (Fig. 1C). Next, the guidewire and inner dilator were removed, allowing the Memokath stent to be inserted into the sheath positioned just above the stricture's proximal end (Fig. 1D). The sheath was subsequently retracted to expose the entire stent within the stricture. After adjusting the stent's position, the inner mandrel was removed, and up to 30 mL of 55 °C sterile water infused to ensure full expansion of the stent's proximal end (Fig. 1E). The stent's proximal end opens into a funnel shape, resting on and anchoring to the stricture (Fig. 1F) [6].

Postoperative follow-up

Our follow-up protocol comprises serum creatinine, kidneys, ureters, and bladder (KUB) radiography, and kidney ultrasonography at 1, 3, and every 6 months post-procedure. SPECT imaging was performed in all patients 3 months post-stent insertion.

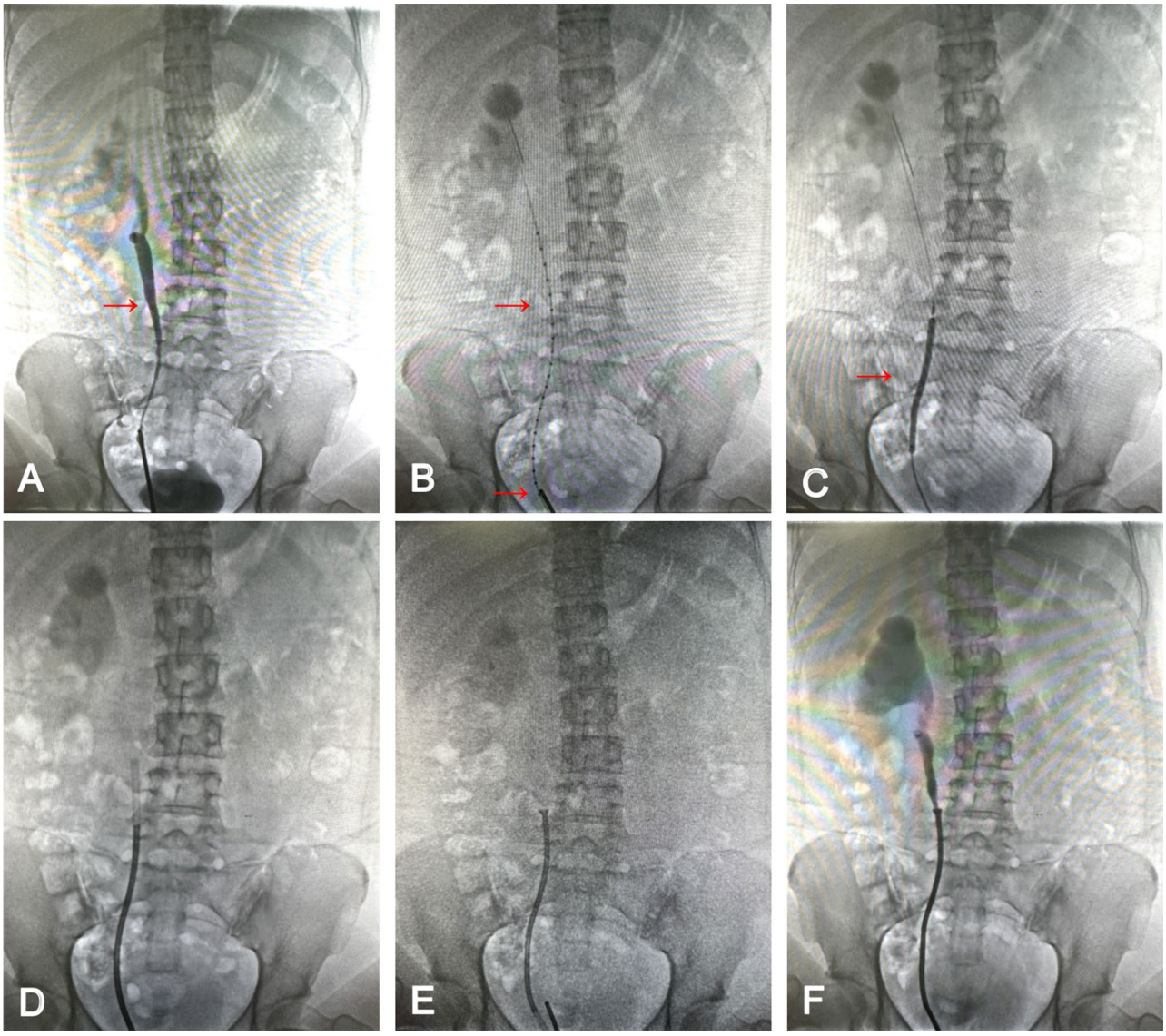

Fig. 1 Step-by-step of insertion of Memokath stent: **A**. retrograde angiography is to clarify the location, length, degree of US and hydronephrosis, etc. **B**. Retrograde insertion of the length-measurement catheter to measure the length of US preciously. **C**. Balloon may be used when encountering severe stenosis. **D**, **E**. Memokath can be inserted and 55ºC of sterile water is infused until full expansion of the proximal end is achieved. **F**. Retrograde pyelography shows excellent ureter patency and excretion

Statistical analysis

The chi-squared test or Fisher's exact test was used to compare categorical variables. The statistical significance of quantitative data was analyzed by Student's t-test or analysis of variance (ANOVA). The Kaplan–Meier method was used for survival analysis. A P value <0.05 was considered statistically significant. All analyses were performed using SPSS software (version 20.00).

Results

Patient demographics and clinical characteristics

This study included 27 patients, patient demographics and clinical characteristics showed in Table 1. All patients underwent a complete course of radiotherapy for gynecological tumors, which included 25 sessions of radiation therapy. Additionally, ten patients received postoperative after-loading radiotherapy. All patients had diffuse US. The mean length of the US were 10.14±6.76 cm (Table 2). The mean volume of hydronephrosis before the procedure was 26.13±5.79 cm^3, while the GFR was 60.96±21.65 mL/min and the creatinine levels were 135.51±122.20 μmol/L before the procedure.

Procedure details

The average procedure time was 52.86±19.09 min, and the average length of hospital stay after the procedure was 4.43±1.83 days. The mean cost of stents and relative fee in our study was CNY 102983.96±8286.42. All 27

Table 1 Patient demographics

Variable		*N*
Total case		27
Age (y)		49.86 ± 10.71
Sex (m/f)		F 27
Height(cm)		157.79 ± 5.13
Weight (Kg)		65.68 ± 9.29
BMI		26.34 ± 3.23
Primary disease (n)		
	cervical carcinoma	19(70.37%)
	ovarian cancer	2(7.40%)
	endometrial carcinoma	6(22.23%)
Adjuvant therapy for the primary disease (n)		
	Combined with RT and chemoradiotherapy	24(88.89%)
	Radiotherapy only	3(11.11%)
Prior treatment for US (n)		
	nephrostomy	7
	double-J	26
	allium stent	5
Interval time between therapy for hydronephrosis and RT (y)		5.35 ± 4.14

US, Ureteral stricture; BMI, Body mass index

Table 2 Clinical data of US and perioperative-related data

Variable		Value
Side of US (n)		
	left	13(48.15%)
	Right	8(29.63%)
	Bilateral	6(22.22%)
Location of US (n)		
	Proximal	1(3.03%)
	Middle	6(18.18%)
	middle and distal	18(54.55%)
	Distal	8(24.24%)
Length of US (cm)		10.14 ± 6.76
Stent insertion approach		
	retrograde	26(78.79%)
	ante-retrograde	7(21.21%)
Time of surgery (min)		52.86 ± 19.09
Hospital stay (d)		4.43 ± 1.83
Average hospitalization cost (CNY)		102983.96 ± 8286.42
Follow-up Time (m)		11.64 ± 5.90
Stent placement success rate		33/33 (100%)
Complication		6(22.22%)
early		
	fever and renal colic	1(3.70%)
later		
	refractory UTI	3(11.11%)
	Migration	1(3.70%)
	Encrustation	0
	stent intolerant	1(3.70%)

Table 3 Analysis between preoperation and 3 months follow-up

Factors	Preoperative	3 months after surgery	*P** value
Hydronephrosis (cm^3)	26.13 ± 5.79	12.73 ± 6.20	< 0.001
Creatinine level (μmol/L)	135.51 ± 122.20	108.87 ± 78.11	0.059
Total GFR (mL/min)	60.96 ± 21.65	69.56 ± 19.48	0.016

*Student's *t* test, relevant index comparison between preoperative and 3 months after surgery

patients (100%) had successful insertion of 33 stents, with six (22.2%) undergoing bilateral ureteral stent placement in one session.

Complications

Early postprocedure complications included fever and renal colic in one patient, which were relieved by medical therapy. Late complications included refractory urinary tract infections (UTIs) in three patients (11.11%), stent intolerance in one patient (3.7%), and stent migration in another patient (3.7%). The stents in patients with late complications were all removed and replaced with nephrostomy treatment.

Follow-up data

The median follow-up time was 13 (IQR: 10−23) months. One patient died from the primary disease while carrying a patent stent. The volume of hydronephrosis significantly decreased (from 26.13±5.79 cm^3 to 12.73±6.20 cm^3; $p<0.001$), and the total GFR significantly increased (from 60.96±21.65 mL/min to 69.96±19.48 mL/min; $p=0.016$) three months after the procedure compared with the measurements before the procedure. The creatinine level three months after the procedure (108.87±78.11 μmol/L) showed a decrease compared with the measurements before the procedure (135.51±122.20 μmol/L; $p=0.059$), but this change was not statistically significant (Table 3). The Kaplan-Meier graph showed that the cumilative patency rate of patients with thermo-expandable metallic stent were 92.4% (SD=5.2%) in eight months, 77.4% (9.1%) in 12 months and 67.7% (SD=12%) in 29 months, while the cumilative survival rate was 87.5% (SD=11.5%) in 29 months, shown in (Fig. 2).

Discussion

Radiotherapy therapy (RT) is an important measure for gynecological tumors, which may subsequently lead to complications such as tissue fibrosis. Ureteral stricture (US) related to gynecological surgery combined with RT is particularly prominent. Some researchers have indicated that the possibility of US is related to whether surgery and the total radiation dose received [11, 12]. Tissue fibrotic response of RT has the characteristic of time-progressive, so that the US usually occurs and develops years after treatments [13]. Some studies suggest that the incidence of US after RT for cervical cancer is about 1.8 -10.3% [14, 15]. As is reported, the risk in the US has increased by 0.15% per year in the 25 years after RT for cervical cancer [16]. In our case, the mean interval time of US needing treatment was 5.35±4.14 years, as similar as other researchers reported was 782.5 (37-2323) days [15].

Memokath stents are of benefit in the treatment of gynecological malignancy patients with a ureteral stricture who need radiation as an aid in end-of-life care. According to our experience, Memokath have excellent performce in situ result from its tight spiral structure with a shaft diameter of 10.5 F. Furthermore, compared to DJ stent, there is no need for frequent replacement and without related LUTS symptom, which has brought improvement of quality of life [17, 18].

The treatment protocol mainly depends on the location and length of the US, prognosis, comorbidities, and even the intention of the patient. The treatment regimen included active monitoring, reconstructive surgery, nephrostomy, and double-J (DJ) stent [19–21]. For the radioactive US, it often has the character of long length, heavy degree of stenosis, and a history of abdominal surgery. Memokath has the merits of strong pressure resistance, diversified models, and easy of placement and

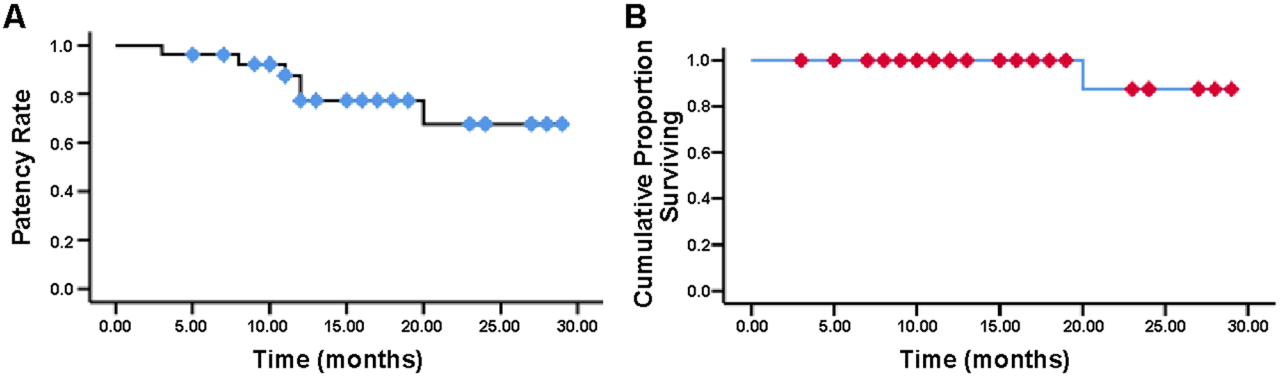

Fig. 2 Kaplan-Meier graph of patency rate (**A**) and survival rate (**B**) about patients

removement, so it is suitable that Memokath stent to treat US after RT [4, 6, 22].

According to our study, all stents were successively inserted. The average operation time and the average operative hospital stay is similar to another research [6]. Memokath stent can be inserted by retrograde and/or anterograde, mostly through retrograde path [23]. However, there were 22% cases underwent retro-anterograde combination path in our study. Combined with relevant literature and our experience, it is believed that retrograde-anterograde way of stent implantation has some advantages: infection control, short drainage path, precise stenosis assessment for impaired renal [24].

As the ureter is not as straight as radiography showed, how to measure length of US precisely? According our experience, the measuring catheter can be used to precisely measure the length of narrow segment (between the two arrows in Fig. 1B), which is helpful to select appropriate length size and models.

Stent complications include migration, stent occlusion and encrustation, stent-related UTI, etc. Our results suggested that the timely patency rate of postoperative stents was 92.86%, similarly with those reported [4]. Early complications included fever and renal colic, with an incidence of about 7.14%, while symptoms relief after conservative treatment. Related study reported that the effectiveness of Memokath is 40 -75% [25], with the incidence of stent encrustation is <10%, stent migration<20%, and stent-related UTI are approximately 7% [26]. In our study, the long-term stent patency was 81.48%, and the late complications included refractory UTI in three case (11.11%), one case of stent migration (3.70%), and another one of stent intolerance (3.70%). In the other two patients, Memokath stents were removed and treated with nephrostomy or D-J tube. According to some literature, the median Memokath stents lifespan was 12-14.5 months in previous study [27].

Nowadays, there is few studies about Memokath stent for change of GFR and hydronephrosis. In our study, the volume of postoperative hydronephrosis was significantly reduced compared with that before surgery, both of them were statistically significant; creatinine levels have an improvement, but no statistical difference. It indicates that Memokath stent can effectively improve the ureteral obstruction and renal function.

Our study had several limitations. First of all, we did not further compare the efficacy and safety of other treatments with Memokath stents. What's more, the retrospective nature and the relatively small patient population of this study have their own inherent limitations. Last but not least, many patients received radiation therapy at other institutions, it was not possible to trace and record the specific radiotherapy doses. Further studies and multi-center studies are required to evaluate the long-term outcomes of Memokath stent for radioactive US. However, our study fills the gap of the Memokath stents in ureteral stenosis after radiotherapy for gynecological tumors.

Conclusion

In our study, it has demonstrated that Memokath stent is effective and safe for patients with ureteral stricture following surgery and radiotherapy with or without chemotherapy for gynecological tumors. Memokath stent has the characteristics of improving hydronephrosis and renal function caused by ureteral obstruction with few complications.

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Author contributions
GX and JT were responsible for study design, coordination, analysis and interpretation of data, as well as supervising the study. YX, ZC, and SC conducted the majority of the study and statistical analysis while also contributing to manuscript drafting. QX, ZZ, HZ, and NL were involved in data collection. All authors reviewed and approved the final manuscript.

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Data availability
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The study was conducted following the Declaration of Helsinki and was approved by the ethics committee for medical research at the Fifth Hospital of Guangzhou Medical University. The need for written informed consent was waived by the Fifth Hospital of Guangzhou Medical University ethics committee due to the retrospective nature of the study.

Consent for publication
Not applicable.

Clinical trial number
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Urology, Key Laboratory of Biological Targeting Diagnosis, Therapy and Rehabilitation of Guangdong Higher Education Institutes, The Fifth Affiliated Hospital of Guangzhou Medical University, Guangzhou Medical University, Guangzhou 510700, China

[2]Guangdong Provincial Key Laboratory of Urology, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou Medical University, Guangzhou 510230, China
[3]Department of Hospital Infection Control, Huangpu District Hospital of Traditional Chinese Medicine, Guangzhou 510799, China
[4]Department of Interventional Radiology, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou 510080, China

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