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# Surgical treatment of the stricture of the lower third of ureter after radiation therapy of pelvic organs

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*Postradiation obstructive changes of distal parts of the ureter most commonly occur after radiation therapy for cervical cancer, endometrial cancer, bladder cancer. Pathogenesis of postradiation lesions of the ureteral wall are explained by destructive effects of radiation on the basal membranes of the capillary cell, causing an occlusion, thrombosis, and neovascularization, which in turn leads to proliferation of fibroblasts and stromal fibrosis. Possible complications include hematuria, urinary tract infections, vesicoureteral reflux, stent migration, stent encrustation. By the way, presence of the stent is often associated with pain and discomfort in patients. Aim of this work is to improve the results of treatment of strictures of the lower ureter following radiotherapy, by evaluating effectiveness of extravesical uretherocystoanastomosis and Boari procedure.*

***Key words:*** *stricture of the lower third of the ureter, post radial obstructive changes, extravesical uretero-cysto-anastomosis, Boari procedure*

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## Introduction

Post-radiation obstructive changes in the distal parts of the ureter comprise 33.6 % of all long-term urological complications of radiation therapy of the lower pelvis [1]. Most commonly, this pathology develops after beam therapy of cervical, endometrial, and bladder cancers [2]. Ureteral strictures are ischemic in respect to the mechanism of development. Pathogenesis of a post-radiation injury of the ureteral wall is attributed to the damage upon basement membranes of cells of capillaries leading to occlusion, thrombosis, and neovascularization, which in turn lead to proliferation of fibroblasts and development of stroma fibrosis [3]. The time period of ureteral damage development can be anything from 6 months to 20 years after radiation therapy of the lower pelvis, and every year the risk increases by 0.15 % [4].

After radiation treatment, blood flow and regeneration ability of the tissue decrease, which considerably limits the range of possible treatments. Currently, there isn»t a standard approach to treatment of patients with post-radiation ureteral obstruction. Treatment selection must take into account the length of the defect and patient»s general somatic status.

Long-term stenting of the ureter is usually applied in somatically preoccupied patients with contraindications for major surgery [5]. Duration of stenting is determined individually per indications. Polymer stents should be changed every 3 months. Metallic stents are less subject to encrustation, so they can be changed once in 12 months, but in patients with post-radiation strictures their effectiveness is decreased [6, 7]. A positive effect (decreased dilation of the pyelocaliceal system and decreased serum creatinine level) during long-term stenting is observed only in 45.5 % patients with post-radiation strictures of the ureter.

Possible complications include hematuria, infections of the urinary tract, vesicoureteral reflux (VUR), stent migration, stent encrustation, and, additionally, stents often cause patients pain and discomfort [5, 8].

Unfortunately, effectiveness of endoureterotomy and balloon dilation in treatment of post-radiation ureteral strictures is extremely low due to defective regeneration in the irradiated tissue of the ureter [9–11, 7].

In somatically healthy patients, open and laparoscopic interventions are possible: ureteroneocystostomy, psoas-hitch, Boari flap which are highly effective for treatment of post-radiation strictures of the ureter. Ureteroneocystostomy is indicated in patients with short (up to 5 cm) distal strictures of the ureter. Ureteral reimplantation should be performed with antireflux protection [12]. There»re several antireflux techniques including intravesical (Cohen procedure), transvesical (Politano-Leadbetter ureteral reimplantation), and extravesical (Lich-Gregoir procedure) techniques.

If the defect is long enough for an anastomosis during ureteral reimplantation, a psoas hitch technique can be used which allows to compensate for 5–10 cm of the defect. The psoas hitch is based on mobilization of the bladder into the retropubic space with subsequent fixation to the psoas tendon [13]. This technique is contraindicated in patients with *Microcystis*. Possible complications include recurrent ureteral strictures and psoas syndrome caused by intraoperative injury of the genitofemoral nerve [14].

For treatment of pronounced defects of the distal parts of the ureter when ureteroneocystostomy is impossible, the alternative is a Boari flap. The Boari flap allows to bridge 10–15 cm of the defect [15]. The Boari flap includes tubularization of a flap from the anterior lateral wall of the bladder with subsequent ureteroneocystostomy with antireflux protection. The Boari flap is often paired with the psoas hitch. The most common complication of the Boari flap is recurrent ureteral stricture.

For long ureteral strictures, as well as ineffective previous interventions, various types of ureteral plastic surgery

using the bowel can be performed. Most commonly, an ileum flap is used as a substitute [16–23]. Contraindications for ileal ureteral substitution are serum creatinine level > 2 mg/dl, neurogenic bladder dysfunction, inflammatory disorders of the intestine, radiation enteritis [24]. Some authors suggest that anastomosis can be formed without antireflux protection, and peristaltic waves of the ilium can prevent reverse urine flow [23, 25, 26]. Other authors state that ileal ureteral substitution with antireflux mechanism is preferable [27–29].

Standard antireflux techniques are associated with an increased risk of strictures at the anastamosis. As a solution, a technique involving formation of an ileo-psoas tunnel was proposed [22]: The distal part of the upper third of the ureter is fixed between the psoas muscle and a segment of the ileum which allows to create antireflux protection. It was shown that ileal ureter with the ileo-psoas tunnel is highly effective in patients with ureteral strictures, because it allows to achieve considerable improvement of renal function with minimal risk of recurrence and long-term complications [30].

Therefore, the problem of optimal treatment of post-radiation ureteral strictures remains unsolved.

**The study objective** is to improve results of treatment of strictures of the lower third of the ureter caused by radiation therapy by evaluating effectiveness of extravesical ureterocystostomy and the Boari flap.

## Materials and methods

In 2007–2015, 192 female patients (aged 22–49) were treated at the Research Institute of Urology and Interventional Radiology named after O.N. Lopatkin for strictures and obliteration of the lower third of the ureter. In all cases, strictures and obliterations were caused by radiation therapy of the lower pelvis for treatment of oncological diseases of the reproductive system (predominantly, cervical cancer). Patients were divided into 3 groups in respect to the type of surgical intervention.

The 1st group ($n = 49$) included patients with ureteral defect shorter than 4 cm who underwent extravesical ureterocystostomy (Barry technique) (Fig. 1).

The 2nd ($n = 45$) and 3rd ($n = 98$) groups included patients with ureteral defect of 4–15 cm, who underwent the Boari flap with and without antireflux protection, respectively (Fig. 2).

The Boari flap without antireflux protection doesn»t include formation of a submucosal tunnel in the flap, the ureter is connected to the flap end-to-end.

Median follow up duration was 38.2 (12–96) months. Renal function (using radioisotope renography), number of attacks of chronic pyelonephritis a year, number of recurrent strictures or obliteration of the ureter, number of cases of clinically significant TUR were evaluated.

It should be noted, that 180 (93.75 %) patients with strictures and obliterations were previously hospitalized with nephrostomy drainages installed due to acute obstructive pyelonephritis. The rest 12 (6.25 %) patients (with strictures) were prepared for surgery without nephrostomy because at the time of surgery they didn»t have any symptoms of chronic pyelonephritis attack.

Statistical data analysis was performed using the Statistica 6.0 software. Median, 25th and 75th percentiles (25 %:75 %) were used for data processing. Significance of differences between quantitative characteristics in the dependent groups (before and after treatment) were evaluated using the Wilcoxon test. Significance level was evaluated using the $\chi^2$-test.

## Results

In the 1st group ($n = 49$), in 47 (96 %) patients after extravesical ureterocystostomy full ureteral patency was restored, while in 2 (4 %) patients, recurrent strictures of the lower third of the ureter were observed 1 month after removal of the internal stent. In both cases, the Boari flap was performed with positive outcome.

Median renal function decrease before and after the surgery was 34 % (22.00:58.50) and 32 % (15.75:39.00), respectively. No statistically significant difference in the level of deficiency in the renal secretion was observed in this treatment group ($p \geq 0.05$).

The majority of patients ($n = 40$) denied attacks of chronic pyelonephritis in the postoperative period. Only in 7 patients one-time pyelonephritis was reported in a year after the surgery.

No clinically significant cases of TUR were observed in this group.

In the 2nd group ($n = 45$), full restoration of the ureteral patency was observed in 43 (95.5 %) patients after the Boari flap with antireflux protection. In 2 (4.5 %) patients, strictures of the ureterovesical anastomosis (connection between the ureter and the bladder flap) were observed 2 months after removal of the inner stent which required direct ureterovesical anastomosis without antireflux protection.

Median renal function decrease before and after the surgery was 44 % (28.00:61.75) and 38 % (16.00:42.00), respectively. In this group, there also weren»t any statistically significant differences in renal secretion deficiency before and after the treatment ($p \geq 0.05$).

Forty patients didn»t experience any pyelonephritis attacks in the postoperative period. Three patients noted one-time attacks of chronic pyelonephritis during the 1-year follow up period.

No clinically significant cases of TUR were observed in this patient group.

In all patients of the 3rd group ($n = 98$) who underwent the Boari flap without antireflux protection, full restoration of the ureteral patency was observed.

Median renal function decrease before and after the surgery was 46 % (31.00:65.00) and 45 % (32.00:61.00),

respectively. In the 3rd group, no statistically significant differences in the level of deficiency in the renal secretion were observed ($p \geq 0.05$).

In 80 patients, there were no attacks of chronic pyelonephritis in the postoperative period. In 15 patients, one-time episodes were observed, in 3 patients – 2 attacks in 1 year.

In 5 patients, clinically significant TUR after the treatment was reported, accompanied by frequent attacks of chronic pyelonephritis (1–2 times a year) and a decrease in renal function by 10 % compared to the initial level.

## Discussion

One of the main difficulties in treatment of patients with post-radiation injuries of the ureter is the risk of recurrence associated with trophic changes in the tissue. Recurrent strictures and obliterations are usually longer which leads to increased scale of surgical interventions, up to ileal ureteral substitution. A reasonable choice of the treatment method is extremely important in these patients and requires special consideration.

In this study, a positive treatment effect was observed in the majority of female patients, including in the long-term postoperative period: improvement or stabilization of renal function, restoration of ureteral patency, removal of nephrostomy drainage.

Results of this study confirm the literature data on the effectiveness of extravesical ureterocystostomy in treatment of strictures of the distal parts of the ureter [32–34]. The recurrence risk in the postoperative period was 4 %, which is consistent with results of other authors [32]. The rate of pyelonephritis attacks was 14.28 %. Results of this work show that extravesical ureterocystostomy is the optimal technique for treatment of strictures and obliterations of the ureter if the defect is shorter than 4 cm.

The question of advisability of using the antureflux technique in the Boari flap remains ambiguous. Some authors recommend using antireflux protection for achieving the optimal treatment outcome [35], while others demonstrate the opposite results [36]. Results of this study show that the Boari flap without antireflux protection allows to prevent recurrences of ureteral strictures, but it is associated with the risk of TUR (5.10 %) and high rate of chronic pyelonephritis attacks (18.36 %). For the Boari flap with antireflux protection, the recurrence risk is 4.44 %, and the rate of pyelonephritis attacks decreases to 6.66 %. Statistical analysis has shown that the differences in the rates of TUR and pyelonephritis attacks were insignificant between the 2nd and 3rd groups. Difference in the recurrence rate in the postoperative period had low statistical significance (see Table).

*Complication of the Boari flap with and without antireflux protection*

| Characteristic | 2nd group ($n$ = 45) | 3rd group ($n$ = 98) | $p$ |
|---|---|---|---|
| Number of patients with recurrent strictures/ obliterations | 2 (4.44 %) | 0 (0 %) | < 0,05 |
| Number of patients with vesicoureteral reflux | 0 (0 %) | 5 (5,10 %) | > 0,05 |
| Number of patients with pyelonephritis attacks | 3 (6.66 %) | 18 (18,36 %) | > 0,05 |

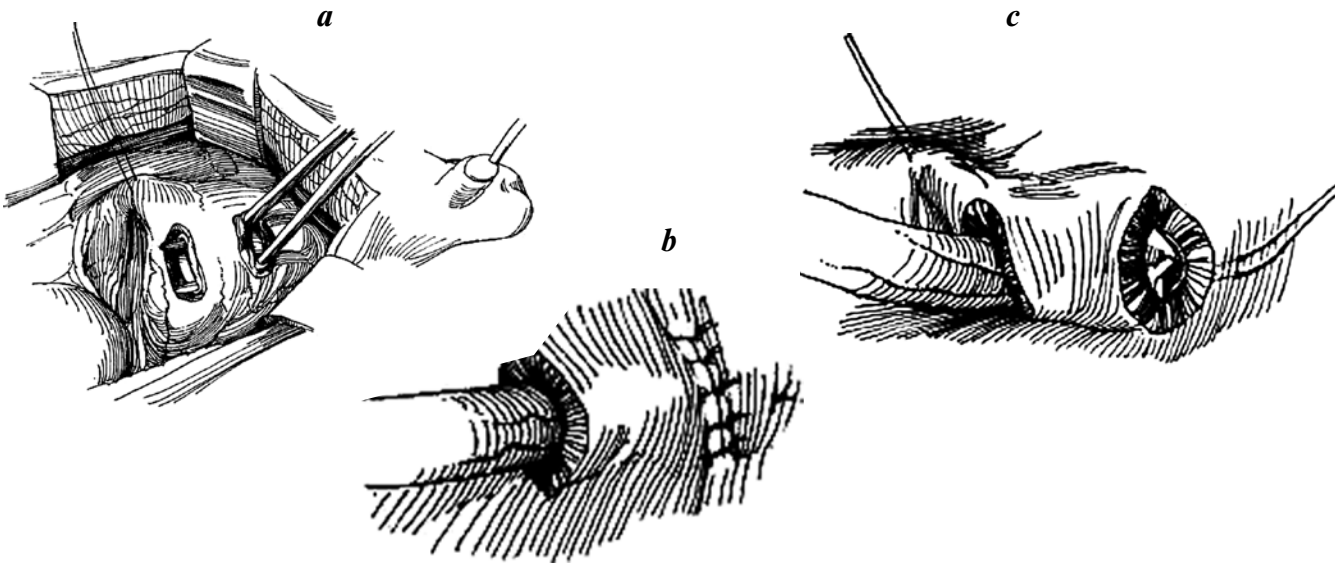


**Fig. 1.** *Barry technique: a – formation of the submucosal tunnel; b – passage of the ureter into the submucosal tunnel; c – connection of the distal part of the ureter with the bladder mucosa, bladder closure [31]*

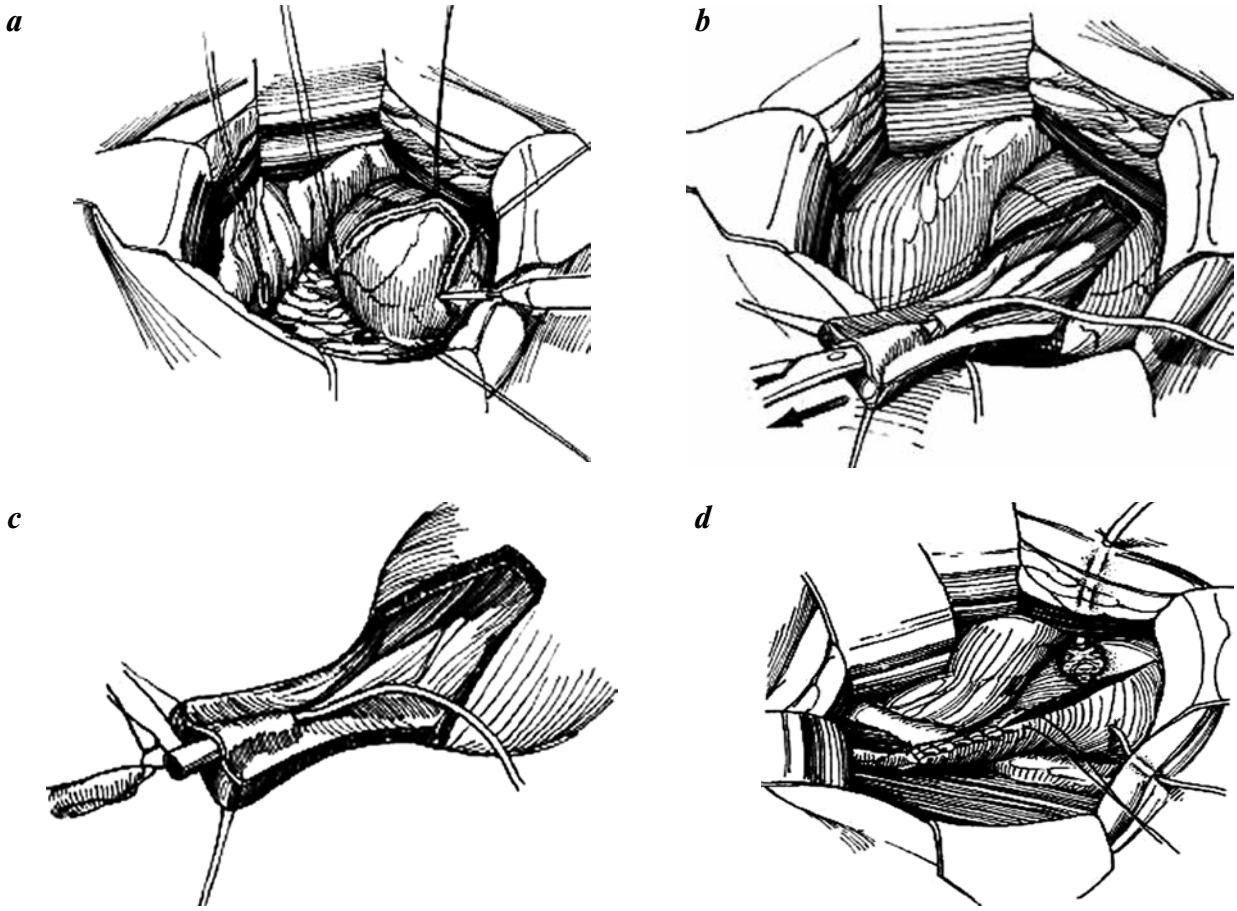


**Fig. 2.** *Boari flap: a – formation of the bladder flap; b – formation of the submucosal tunnel in the flap; c – passage of the ureter into the submucosal tunnel; d – flap and bladder closure on the internal stent [31]*

Therefore, use of the antireflux technique during the Boari flap in patients with 4–15 cm post-radiation strictures and obliterations of the ureter doesn't significantly affect treatment outcome.

## Conclusion

Extravesical ureterocystostomy is the optimal technique for treatment of strictures and obliterations of the ureter in patients after radiation therapy if the defect is shorter than 4 cm.

In patients with post-radiation strictures and obliterations of the lower third of the ureter ranging from 4 to 15 cm in length, the Boari flap is advisable. The use of antireflux technique during this intervention doesn't affect the outcome of the treatment.

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