

# Management of bladder cancer with Studer orthotopic neobladder: 13-year experience

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## Abstract

**Background:** We present the results of patients submitted to a Studer type urinary orthotopic derivation after radical cystectomy.

**Methods:** The files of patients with bladder cancer submitted to a radical cystectomy plus the procedure of the ileal neobladder were reviewed in our hospital from January 1992 until December 2004. Patients were divided into two groups: group A—60 years old or younger and group B—>60 years old.

**Results:** From 306 patients submitted to radical cystectomy with urinary derivation, there were 42 patients (13.7%) included with Studer type neobladder. There were 34 (80.9 %) men and 8 (19.1%) women, with an average age of 60 years. Average surgical time was 7 h with an average blood loss of 1600 cc requiring transfer to intensive care unit (ICU) in 55% of the cases. The most frequent early complication was metabolic acidosis that was present in 28 (66%) patients. The most severe complication was ileal-ureter urinary leak, which was present in seven (16.6 %) patients. Among the most frequent late complications are the day- and night-time urinary incontinence often related to urinary infections and intestinal occlusion. Overall 5-year survival was 71%, cancer-specific mortality was 15% and surgical-related mortality was 7.3%.

**Conclusions:** The performance of procedures with orthotopic neobladders is actually feasible in experienced hospital centers and is a valuable alternative to urinary heterotopic derivation with ileal conduit. Postoperative patient management and regular follow-up is of major importance.

**Key words:** bladder cancer, radical cystectomy, orthotopic neobladder.

## Introduction

Urinary diversion through ileal conduit has been regarded as the standard procedure after radical cystectomy from bladder cancer. However, in the last 20 years other aspects have gained interest, mainly regarding patient's body image and quality of life through the use of substitute orthotopic bladders.<sup>1</sup>

The first orthotopic bladder reconstruction in humans was described by Lemoine in 1913.<sup>2</sup> In 1979, Camey and Le Duc reported their experience with neobladder creation from small intestine while preserving the urethral sphincter during cystectomy.<sup>3</sup> In 1985, Studer et al. published their first experience with low-pressure orthotopic neobladder (ONB) replacement in animals.<sup>4</sup>

ONB shares several characteristics with normal bladder such as a continence mechanism, an appropriate capacity with low vesical pressure when full and an anti-reflux mechanism to prevent dilation and damage to the upper urinary tract.<sup>5</sup> Tissue from the stomach or small and large intestine or a combination of these has been used for its creation.<sup>6,7</sup> Use of small intestine tissue has become a standard because of its compliance and better performance when subjected to pressure.

ONB replacement is carried out in several specialized centers as an option for some patients, being one of the best alternatives for urinary diversion. However, this procedure is perceived as technically difficult and is associated with a high preoperative morbidity rate and long-term complications.

The main contraindications for ONB replacement are prostatic urethral cancer, urethral stenosis, impossibility for long-term follow-up and inflammatory bowel disease affecting selected intestinal segments.<sup>8</sup>

ONB replacement has some anatomic, physiological and social advantages and has been regarded as the standard procedure in specialized reference centers. Here we present 13 years of experience with the Studer-ONB replacement at the Oncology Hospital, 21<sup>st</sup> National Medical Center of the Mexican Institute of Social Security in Mexico City.

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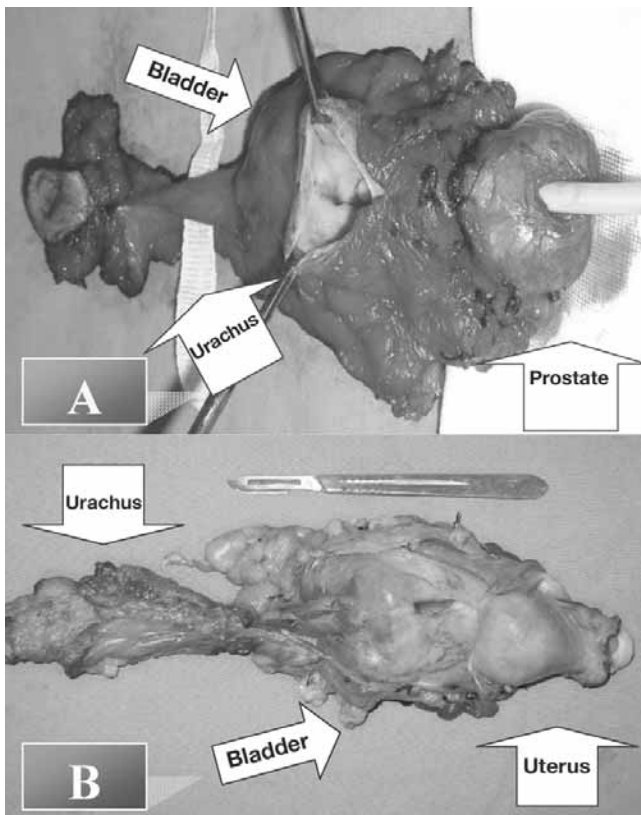
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## Materials and Methods

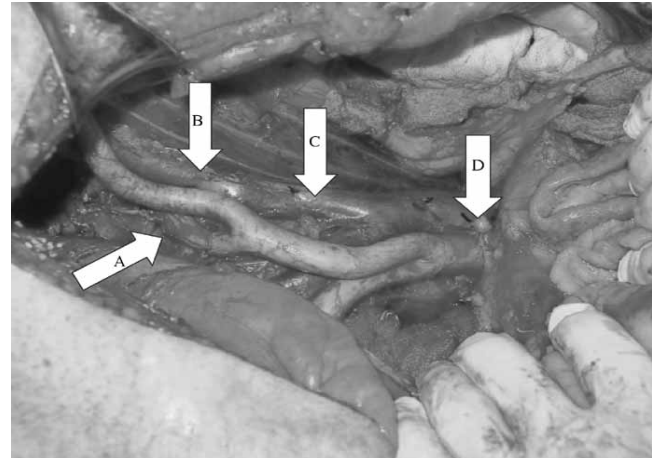
We carried out a retrospective, descriptive and observational study. We reviewed clinical files of all patients with bladder cancer treated with radical cystectomy in our Urology Service from January 15, 1992 to December 18, 2004, selecting only those patients who received Studer-type orthotopic urinary diversion. Patients were classified into two groups: Group A—patients <60 years old and Group B—patients >60 years old.

Chest x-ray, abdomino-pelvic CT, cystoscopy, transurethral resection of bladder (TURB) and manual exploration we carried out on all patients preoperatively. Patients underwent radical cystectomy (Figure 1) with standard lymphadenectomy (pelvic, internal and external iliac ganglia) between January 1992 and December 2002. Extensive lymphadenectomy (which includes common iliac, presacral, paracaval, intercaval aortic and para-aortic ganglia as well as high ligation of the inferior mesenteric artery) was performed between January 2003 and December 2004 (Figure 2) adding Studer-type orthotopic urinary diversion (Figure 3).

Technique includes placement of two urethral catheters (feeding tubes 6 Fr) exteriorized through the midline of the infraumbilical suture, two Penrose-drains exteriorized to the iliac fossae, one



**Figure 1.** Radical cystectomy pieces from urachal cancer towards the bladder. (A) Male: prostate, bladder and urachus. (B) Female: uterus, bladder and urachus.

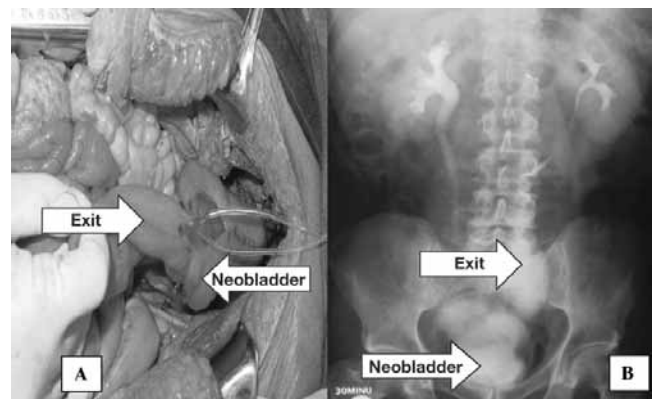


**Figure 2.** Extensive lymphadenectomy including pelvic resection, internal iliac ganglia (A), external iliac ganglia (B), common ganglia (C) and high ligation of the inferior mesenteric artery (D).

transurethral catheter (TUC) (20 Fr) and one neocystostomy tube (20 Fr). Urethral catheters were removed 10 days postoperatively, and abdominal drains were removed 1 day later. Neocystostomy was removed 2 weeks postoperatively and TUC was removed 1 week later.

Once tubes, catheters and drains were removed, the patient was informed about general procedures for micturition such as spontaneous micturition and to empty the bladder every 3 h during the day and night with special attention to the first weeks where bladder capacity increases gradually, as well as to carry out Credé's maneuver for maximum emptying. Residual urine was managed with intermittent clean catheters.

The following parameters were analyzed: age, gender, smoking, previous TURB, clinical and pathological TNM stages, histological type, bleeding, surgical time, presence of metastatic ganglia, type



**Figure 3.** (A) Studer-type macroscopic view including exit and neobladder reservoir. (B) Image from excretory urography of same patient 4 months after the procedure.

of lymphadenectomy, ICU support after surgery, requirement of total parenteral nutrition (TPN), mortality and survival.

For statistical analysis, we used SPSS v.12 (Chicago, IL), carrying out a multivariate logistic regression analysis as well as Kaplan-Meier curves to measure independent factors related with survival.

## Results

A total of 42 (13.7%) patients diagnosed with bladder cancer underwent radical cystectomy and Studer-type urinary diversion in our hospital over a period of 13 years.

Of these patients, 34 (80.9%) were males and 8 (19.1%) females with an average age of 60 years (range: 39-82 years). They were classified into two groups: group A, <60 years old and group B, >60 years-old. Each study group was comprised of 21 patients (Table 1).

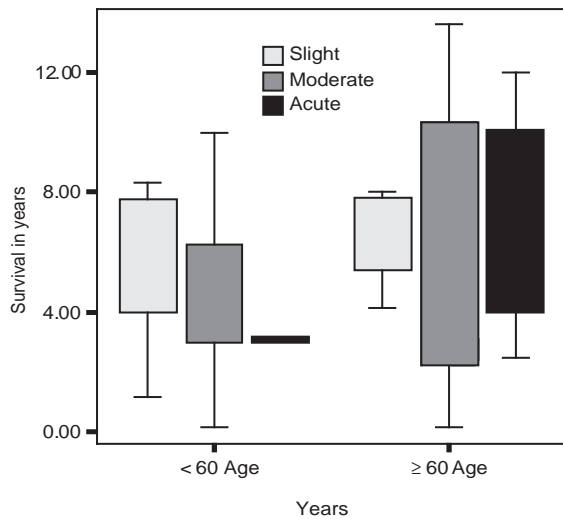
Of the patients, 46% were heavy smokers. We observed 12% of patients clinically reported as T3 were, in fact, pT2; 61% of cases had a confined organ disease and 9.5% of cases had no documentation about tumor activity in the final report (pT0).

Average surgical time was 7 h with an average blood loss of 1600 cc in all patients. However, group B reported an average blood loss of 350 0ml (Figure 4). ICU support was required in

**Table 1.** Results analysis

		Age of patients	
		<60 years (Group A)	>60 years (Group B)
Sex	Male	19	15
	Female	2	6
Smoking	Yes	15	14
	No	6	7
Previous TUBR	1	10	11
	2	8	7
	3 or more	3	3
TNM	T1N0M0	5	3
	T1N1M0	0	1
	T2N0M0	8	10
	T2N1M0	2	1
	T3N0M0	1	2
	T3N1M0	3	2
	Pt0	2	2
Bleeding	<1000 ml	5	4
	1000-2000 ml	14	8
	>2000 ml	2	9
Surgical time	<5 h	3	2
	5-7 h	7	10
	>7 h	11	9
Nodes	Positive	6	3
	Negative	15	18
Lymphadenectomy type	Standard	14	19
	Extensive	7	2
ICU	Yes	7	15
	No	14	6
TPN	Yes	10	16
	No	11	5
Histological type	Urothelial	13	12
	Bladder adenocarcinoma	1	2
	Urachal adenocarcinoma	1	2
	Urothelial/squamous cell	2	1
	Urothelial/micropapillary	2	2
	PT0	2	2
STN 3 years		21	13
STN 5 years		19	11

TUBR, transurethral bladder resection; TPN, total parenteral nutrition; ICU, intensive care unit; OS, overall survival.



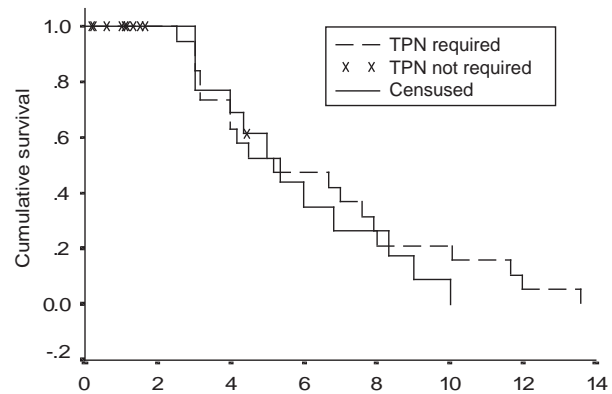
**Figure 4.** Survival in years by age group in relation to intra-operative bleeding.

55% of cases, mainly for surveillance of high risk from a prolonged surgical time (68% of cases belonged to group B).

Of the cases, 61% required TPN and 60% belonged to group B. Although no significant differences were obtained, we determined an unfavorable prognosis trend for patients in group B (Figure 5).

As for morbidity, the most frequent minor complication was metabolic acidosis in 28 (66%) patients, followed by elongated ileum in 15 (35%) patients. Other minor complications were lymphorrhea and pneumothorax. The most frequent major complication was uretero-ileal urinary leakage in seven (16.6%) patients, of which five required a second surgery.

As for late minor complications, the most common were erectile dysfunction (35%), night urinary incontinence (28%), day urinary incontinence (21%) and repeated urinary tract infections (21%). The late major complications were intestinal



**Figure 5.** Kaplan-Meier curve showing the relation between survival and requirement of total parenteral nutrition (TPN).

occlusion (7.1%), pulmonary thromboembolism (4.7%) and chronic renal insufficiency (2.3%).

During a 13-year follow-up period, 12 (28%) patients underwent a second surgery. It is important to highlight that these complications occurred in 50% of patients during the first 3 years of experience using this technique and some patients presented two or more major early complications (Table 2) and late complications (Table 3).

Nine patients (21%) with positive ganglia received therapy. The first group (five patients) was treated with methotrexate, vinblastine, doxorubicin and cisplatin (MVAC). Histological types were two urothelial, one adenocarcinoma, one urothelial/squamous cell and one urothelial/micropapillary. Three patients received only 2/5 cycles because of high toxicity. Only two patients completed the regime and programmed cycles. Only one patient who received the full treatment achieved a 5-year survival, the others presented progression and died from the disease (these patients had been subjected to standard lymphadenectomy). The second group with four patients received five cycles of gem-

**Table 2.** Early complications analysis

	n	%	Treatment	
			Conservative	Surgical
1. Metabolic acidosis	28	66.0	28	0
2. Prolonged ileus	15	35.0	12	3
3. Lymphorrhea	10	23.0	10	0
4. Ileo-urethral leak*	7	16.6	2	5
5. Eventration*	6	14.2	2	4
6. Intestinal anastomosis leak*	3	7.1	0	3
7. Pneumonia	2	4.7	2	0
8. Pneumothorax	1	2.3	1	0
9. Erosive gastritis	1	2.3	1	0
10. Perforated duodenal ulcer*	1	2.3	0	1

\*Major complications.

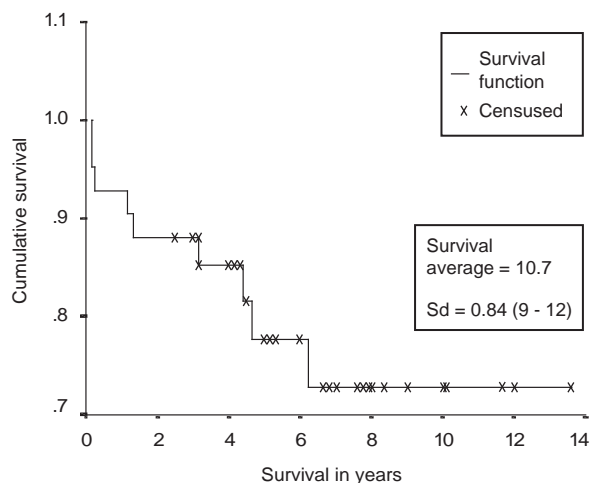
**Table 3.** Late complications analysis

	n	%	Treatment	
			Conservative	Surgical
1. Erectile dysfunction	15	35.0	15	0
2. Nocturnal incontinence	12	28.0	12	0
3. Daytime incontinence	9	21.0	8	0
4. Repeated UTI	9	21.0	9	0
5. Intestinal subocclusion	8	19.0	5	3
6. Metabolic acidosis	6	14.0	6	0
7. Severe urinary retention	4	9.5	4	0
8. Intestinal occlusion*	3	7.1	0	3
9. VUR	3	7.1	3	0
10. Postincisional hernia	2	4.7	1	1
11. PT*	2	4.7	2	0
12. Uretero-reservoir stenosis	2	4.7	0	2
13. Uretero-ileal stenosis	1	2.3	0	1
14. CRI*	1	2.3	0	0

\*Major complications. UTI, urinary tract infection; VUR, vesicoureteral reflux; PT, pulmonary thromboembolus; CRI, chronic renal insufficiency.

citabine/cisplatin, which was well tolerated by all of them. They underwent extensive lymphadenectomy. Two patients with urothelial/micropapillary relapses were alive after a 5-year follow-up, and the other two patients had disease progression and died from the disease. The most frequent locations for metastatic tumors were non-regional lymphatic nodes (para-aortic), lung, liver and bone.

Overall 5-year survival was 71%, overall cancer-specific mortality was 15% and surgery-related overall mortality was 7.3% (Figure 6).



**Figure 6.** Kaplan-Meier graph representing survival in years in relation to cumulative survival.

## Discussion

To create a urinary reservoir, tissues from stomach, small intestine and colon have been used, either alone or combined. Ileum has shown advantages over other segments because of its lower contractility and higher distensibility, which provides better continence than orthotopic neobladders made of large intestine. There is evidence that colon tissue presents less distensibility and stores urine at higher pressures than small intestine. The two most widely used orthotopic diversions were described by Studer and Hautmann. Studies focused on ileal neobladders show they have a volume capacity comparable to colon neobladders; pressure with maximum capacity is smaller in ileum neobladders, resulting in better urinary continence.<sup>1</sup>

Paananen et al. compared clinical, enterocystometric and urofluxometric characteristics of orthotopic urinary diversions carried out in patients with bladder cancer including 78 male patients; 66 had ileal neobladder (30 Studer, 24 Hautmann and 12 T-shaped bag) and 12 patients had right colon urinary reservoirs. They found no significant differences in enterocystometry evaluation between ileal and colon urinary diversions as for volume and base pressures, except for magnitude of contractions, which were higher in colon reservoirs than ileal.

Urofluxometry showed smaller empty volume, lower speed for maximum flux and higher volume of residual urine in colon diversions than in ileal diversions.<sup>9</sup>

To build an orthotopic neobladder, a reservoir is necessary that stores an appropriate urine volume with low pressure and limited solute absorption, as well as rhabdosphincter and smooth sphincter. Basic principles include sphere-shaped reservoir made

from several folded ileum segments open at their antimesenteric border with a capacity ~500 ml without mechanical obstruction from a cone-shaped reservoir or residual prostatic tissue.<sup>1</sup>

In 1989, Studer et al. reported their initial 3-year experience on orthotopic neobladder replacement,<sup>10</sup> and their most recent study includes 20 years of experience on orthotopic neobladder replacement in 400 patients, demonstrating the permanency of this procedure.<sup>1</sup>

Studer-type neobladder is a replacement made from a long segment of ileal tissue, detubularized, isoperistaltic and afferent. It is obtained through isolation of 55-60 cm of terminal ileum at 25 cm of the ileocecal valve. From the segment, 40-45 cm are used for reservoir and 15 cm are used to build the tubular afferent and carry out ureter anastomosis.<sup>11</sup>

In the last 15 years, radical cystectomy with orthotopic neobladder is replacing ileal conduit in some specialized centers and has become the standard treatment for urinary diversions.<sup>12,13</sup> In our hospital, 13.7% of radical cystectomies were carried out using Studer's technique during the last 13 years.

Hautmann et al. considered the effect of local relapse in neobladder function, reporting 12% of relapses in 357 patients; however, most (93%) retained normal neobladder function even after relapse.<sup>14</sup>

Stein et al. performed a review of seven studies and reported the incidence of urethral affection in women subjected cystectomy. They found a urethral incidence of 6-46% with an average of 12.4% in 348 women.<sup>15</sup>

One of the main risk factors for urethral affection in women is associated with the bladder neck, although 50% do not present it. The second factor is associated with the vaginal wall.<sup>15</sup> Chen et al. highlighted the need to obtain negative intraoperative margins during cystectomy and found that in 115 female cases, 8% presented urethral involvement.<sup>16</sup>

Other series reports bladder neck and a segment from proximal urethra resection.<sup>13</sup> It has recently been reported that the proximal urethra in women contains only transitional cells and, therefore, can be removed completely and still preserve the continence mechanism.<sup>9</sup>

In Studer's series, 4-5% of patients presented urethral relapse. This can be treated successfully with intraurethral bacillus Calmette-Guerin (BCG) in 80% of patients with in situ cancer. Patients with papillary and transitional carcinomas should be subjected to urethrectomy.<sup>1</sup>

Early complications in Studer's series were associated in 61% cases to cystectomy and in 39% cases to ileal conduit creation. There were 1.8% of fatal complications: septicemia, cerebrovascular accident, AMI and pulmonary thromboembolism, with a significant difference in patients <75 years of age. In our series the main severe complications, although not the most frequent, were ureteroileal urinary leakage, intestinal anastomosis leakage and eventration.<sup>19</sup>

In our series, metabolic acidosis was the most frequent early complication and the sixth most frequent late complication.<sup>1,12</sup> This

is related with the type and length of the ileal segment and storage time where protons are resorbed by urine in Na<sup>+</sup> exchange.<sup>17</sup> Skinner et al. report 150-200 mmol/L serum creatinine is a high risk factor for acidosis as well as having previous surgery, radiotherapy and type of replacement.<sup>18</sup>

In Studer's series, patients with 40-45 cm ileum reservoirs presented metabolic acidosis in the short term and required sodium bicarbonate replacement; however, metabolic acidosis was not present in the long term and renal function was preserved appropriately (serum creatinine <120 mmol/L).<sup>1</sup> In our study, the reservoir was made with a length similar to Studer's, obtaining a bladder capacity of 450 cc at 6 months, reducing the percentage of metabolic acidosis from 66% as an early complication to 14% as a late complication.

Bone mineral density reduction is an alarming long-term effect; however, patients with continent urinary diversions who retain normal renal function rarely present bone alterations. Some prospective studies at 17 years have demonstrated no long-term metabolic acidosis.<sup>19</sup>

Cosnes et al. reported that proximal intestine resection is better tolerated than distal intestine resection.<sup>20</sup> Ileum absorbs 95% of biliary salts and vitamin B12. However, a >60 cm ileum resection seldom impacts this absorption.<sup>21</sup> Ileum resection >100 cm results in severely compromised intestinal absorption.<sup>22</sup>

Studer's series reported no high incidence of urolithiasis, vesicular lithos and diarrhea.<sup>1</sup>

Biliary acid absorption is compromised in patients with extensive ileal resection where the ileocecal valve is removed. Cathartic action of biliary acids in the colon produces diarrhea when it prevents sodium absorption in the colon.<sup>23,24</sup>

Other factors that can promote urolithiasis are dehydration, hypercalciuria, hypersulfaturia and hypocitraturia.<sup>25</sup>

In patients with ileal conduits, toxicity from chemotherapy drugs such as methotrexate, phenytoin, theophylline, antibiotics and others are well documented.<sup>26</sup> Patients undergoing treatment should have an appropriate hydration as well as immediate urine drainage. Diabetic patients tend to present a higher glucose absorption through urinary diversions.<sup>27</sup>

As for continence preservation, Studer reported that 360/400 (90%) of patients presented full continence during daytime and 79% during night time. Of the patients, 93% were able to have spontaneous micturition at the time of their last visit.<sup>1</sup> In our study, day continence rate was 79% and night continence rate was 72%. Other series report similar results.<sup>12,13</sup>

Zehnder et al. demonstrated that urinary tract infections in patients with ileal neobladders produce incontinence and, when treated, the patient returns to basal continence level.<sup>28</sup> Problems associated with emptying are infected urine, incontinence and obstructive uropathy. For a residual volume after micturition >20 ml, use of intermittent clean catheter (ICC) in 7-12% of cases is recommended.<sup>16</sup>

This has been associated with two factors: technical failure when building the neobladder (obstruction when creating a loop)

and secondary obstruction because of mucous that exits with neobladder, residual prostatic tissue and urethral stenosis.

Thurairaja and Studer found that ICC incidence can be reduced if the reservoir is nonconical and if unobstructive surgery is performed.<sup>29</sup> In our study only one patient required ICC and other was converted to ileal conduit due to neobladder ischemia above anastomosis.

Renal dysfunction was presented in the long term in patients with obstructive uropathy documented before surgery. Therefore, some series do not recommend antireflux plasty because of presenting a high rate of stenosis.<sup>1</sup>

There are few comparative studies about quality of life in patients with Studer-type and other orthotopic bladder replacements. Mansson et al. reported a comparative study between ileal vs. colon neobladder and found nonsignificant statistical differences between these procedures. This may be because questions were not related to urinary function and were originally aimed at patients who received chemotherapy.<sup>30</sup> Other authors who focused on renal function have found significant differences in favor of orthotopic neobladder replacement.

In conclusion, orthotopic neobladder is a viable option in patients subjected to radical cystectomy. It is a good alternative for urinary diversion when compared with ileal conduit. It should be carried out by experienced surgeons who will play an important role in the patient's adaptation and follow-up.

This study demonstrates this is a safe technique that can be reproduced with satisfactory long-term results. It provides patients with the opportunity to retain spontaneous micturition as close as possible to anatomical and physiological normality, thus improving their quality of life.

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