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## Ileal Neobladder and Its Variants

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### Article info

#### Keywords:

Antireflux  
Diversion  
Ileum  
Low-pressure reservoir  
Orthotopic neobladder

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### Abstract

Orthotopic neobladder substitution represents an important step in the evolution of urinary diversion. It is now considered the diversion of choice for the majority of patients, both male and female, who undergo cystectomy and is the procedure with which other types of diversion must be compared. Nevertheless, in the preoperative setting, all options for urinary diversion should be explained comprehensively to the patient, along with the potential short- and long-term risks and the beneficial effects of each type of diversion. With regard to the risk of urethral recurrence, the decision to perform a neobladder ultimately depends on the intraoperative frozen section analysis of the distal urethral margin.

Neobladder construction is based on the concept of detubularization and folding to construct a low-pressure reservoir. All parts of the small and large intestine as well as the stomach have been intensely studied for the construction of neobladders. In this respect, there is substantial agreement in the literature that the terminal ileum possesses superior anatomic and functional characteristics.

Given the lack of prospective randomized trials, controversies still exist with regard to the technique for preventing reflux in orthotopic substitutes and the superiority of one neobladder technique over others, provided the detubularized intestinal segment is reconfigured to an adequate-sized spherical reservoir.

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### 1. Introduction

The evolution of ileal neobladder goes back to Rosenberg in 1893, who was the first to experimentally interpose ileum between the ureters and the urethra, and the pioneering work of Le Duc and Camey, who in 1979 reported their first clinical experience with orthotopic bladder substitution [1]. An ileal segment was anastomosed directly to the native, intact urethra of male patients after cystectomy. Shortcomings of this early technique using tubular ileum were the low-volume reservoir with high intraluminal pressure and renal deterioration on the aboral side due to peristalsis.

Modern-day orthotopic diversion most closely resembles the original urinary bladder both in function and location and can be considered a “natural extension” of the

continent cutaneous diversion. Orthotopic reconstruction of the lower urinary tract has emerged in large centers as the most commonly performed type of urinary diversion [2].

Voiding is initiated by Valsalva maneuver, some peristaltic activity, and synchronic relaxation of the pelvic muscle floor. A well-functioning rhabdosphincter, however, is required and must be preserved during dissection [3]. Up to the early 1990s, orthotopic lower-tract reconstruction was contraindicated in females. The main reason for this was that, at that time, the entire urethra was removed in radical pelvic surgery because it was thought to provide essential cancer control; however, the remaining rhabdosphincter proved to be insufficient to provide adequate urinary continence [4].

With growing evidence demonstrating the oncologic safety and technical feasibility of neobladder construction in females [5,6] and distinct anatomic studies on the female rhabdosphincter [7], these studies formed the basis for recommending orthotopic neobladder as the diversion type of choice both in male and female patients.

## 2. Principles of orthotopic urinary diversion

### 2.1. Basic principles

Continent urinary reservoir construction is based on configuration, accommodation, and compliance [8]. Based on Laplace's law, the pressure of a reservoir is defined as  $P = T \times 2D/R$ , in which  $P$  is pressure,  $T$  is the mural tension,  $D$  is the thickness of the wall, and  $R$  is the radius [9]. Thus intraluminal pressure is inversely correlated to the radius of a spherical reservoir. A tubular segment with its small radius will reach already-high kidney-deteriorating intraluminal pressures at low volumes. A spherical reservoir, however, will maintain the largest capacity with the lowest pressure due to a larger radius. Based on the concept of detubularization and folding [10], the shape is also critical for the development of a true spherical configuration resulting in the utmost reduction of internal pressures during filling to a physiologic capacity [8] (Fig. 1).

### 2.2. Which bowel segment should be used for ileal neobladder construction?

Multiple studies have addressed the issue of which bowel segment is ideally suited for orthotopic diversion. One of the main principles of orthotopic diversion is the storage of

urine at the lowest pressure to prevent reflux and incontinence. All parts of the small and large intestine as well as the stomach have been intensely studied for construction of urine reservoirs.

Large-bowel orthotopic substitutes are less compliant than ileal segments and store urine at higher pressures. Schrier et al compared sigmoid and ileal neobladders urodynamically and showed that the ileum had favorable characteristics in terms of larger capacity, lower filling pressures, and improved compliance [11]. Interestingly, in an *in vivo* canine model, it was shown that ileal circular layers were more distensible compared to ceecal circular layers followed by ileal longitudinal layers [12]. The colonic longitudinal layer proved to be indistensible. Another important aspect of ileal segments used for continent diversion is the development of mucosal atrophy in the long term, resulting in less reabsorption of hydrogen and chloride, which seems to be more likely in ileal segments than in colonic segments [13]. Metabolic consequences due to bowel wall secretion and urinary reabsorption from the intestinal reservoir can be best compensated in the terminal ileum compared to the proximal ileum or jejunum (Fig. 2). Collectively, these data clearly show that the terminal ileal segment is the most ideally suited bowel segment for orthotopic urinary diversion [14].

Gastric forms of neobladder have been advocated in the pediatric population and go back to the experiences of Nguyen and colleagues reporting about gastrocystoplasty [15]. In fact, the stomach offers some advantages in certain clinical situations. The excretion of hydrogen and chloride is not only beneficial in patients with compromised renal function but also reduces the risk of recurrent urinary tract infections along with production of less mucus. In addition,

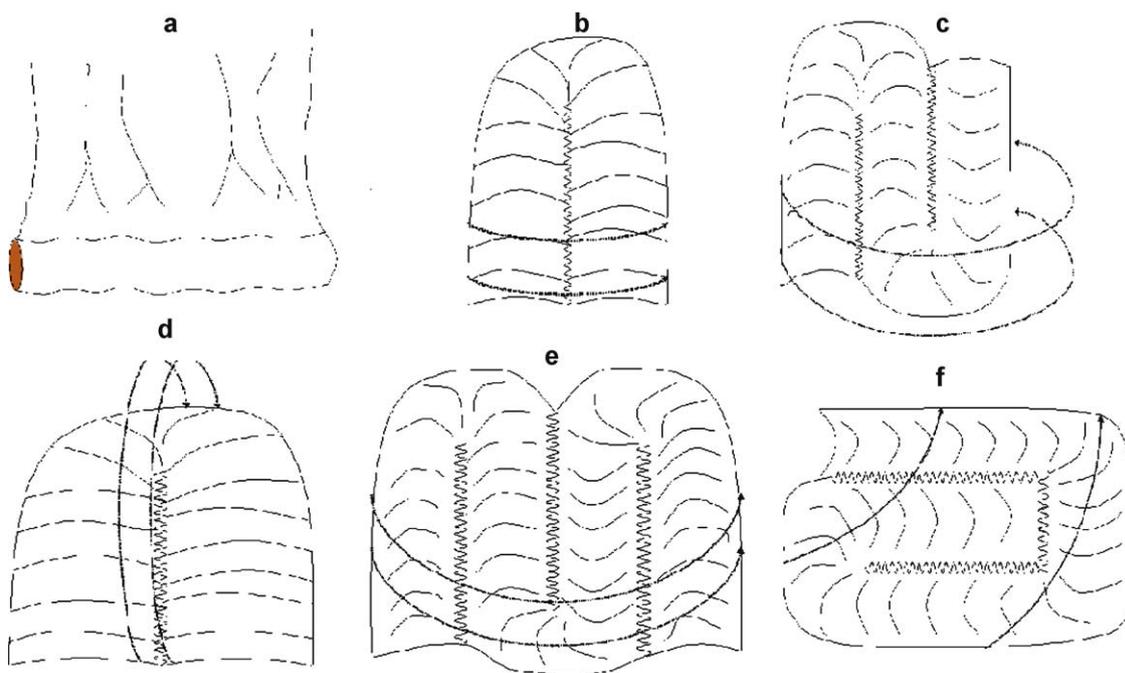


Fig. 1 – Principal methods of transforming intestinal segments into urinary reservoirs: (a) Tubular segment; (b) U-shaped reservoir; (c) S-shaped reservoir; (d) Goodwin principle: folded U-shaped reservoir with and without afferent segment (Studer-pouch, T-pouch, I-pouch); (e) W- or M-reservoir (eg, Hautmann-pouch); (f) circular reconstruction (eg, vesica ileale Padova).

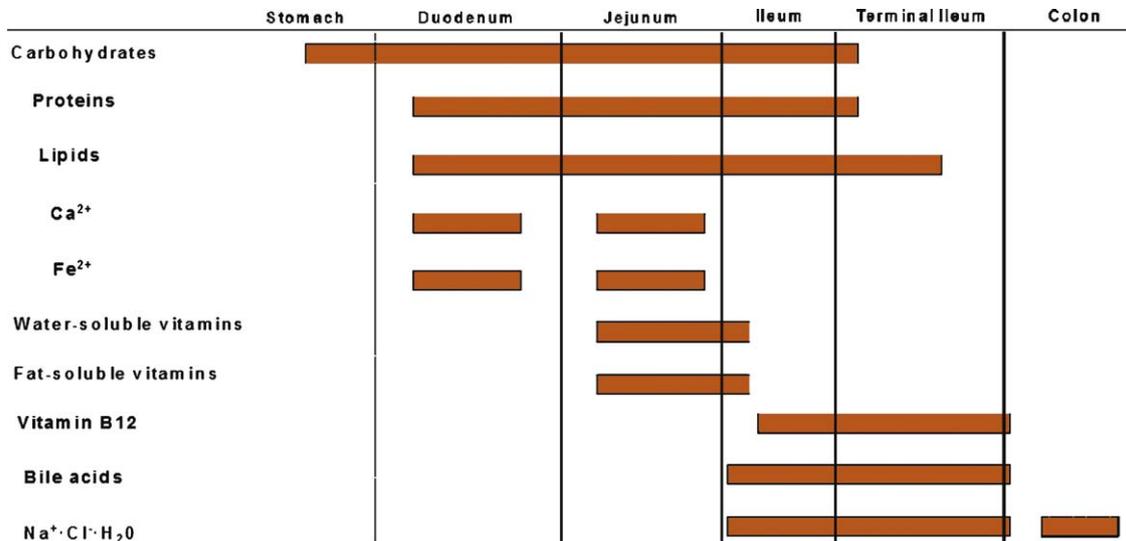


Fig. 2 – Predominant site of reabsorption of nutritional components in different gastrointestinal segments [35].

an antirefluxive ureteral anastomosis is simpler to perform because the muscle wall of the stomach is thicker than that of other intestinal segments. However, electrolyte disturbances such as hypochloric alkalosis may occur in patients with gastric neobladder [16]. Lin et al reported in 2000 on urodynamic long-term results of eight patients with gastric neobladder and found a significantly reduced capacity along with higher incontinence rates [17]. Moreover, hematuria and dysuria, as consequences of urethral irritation by increased urine acidity, have also been reported but may be treated sufficiently with H<sub>2</sub>- or proton pump blockers. Composite neobladders consisting of gastric and bowel segments might reduce some of the disadvantages of gastric neobladders in selected patients [18] (Fig. 3).

### 3. Patient selection criteria

In patients who are eligible for radical cystectomy, an orthotopic diversion should be generally considered as the diversion of choice. Nevertheless, in the preoperative

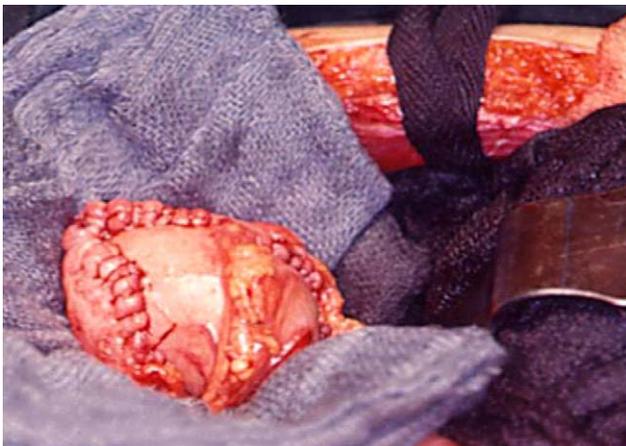


Fig. 3 – Composite pouch using gastroileocolonic segments in a child.

setting, all options for urinary diversion should be explained comprehensibly to the patient, along with the potential short- and long-term risks and the beneficial effects of each type of diversion. The patient must understand that the decision to perform a neobladder substitution ultimately depends on the intraoperative frozen section analysis of the distal urethral margin [19].

With regard to the high accuracy of intraoperative frozen section analysis for detection of malignant urothelial margins at radical cystectomy [20,21], patients with positive margins are at significant risk of urethral recurrence and are not appropriate candidates for orthotopic diversion [19]. Therefore, all patients should be marked preoperatively for a cutaneous stoma by an experienced physician or nurse and also should be instructed how to catheterize a neobladder in case of urinary retention.

Advanced patient age is not necessarily a contraindication for neobladder substitution. Despite recent data demonstrating statistically higher continence rates in patients <70 yr old, several reports provide sufficient evidence for extending the indication for orthotopic diversion to octogenarians as a feasible and safe treatment option, considering individual circumstances. Differentiation between the chronologic and biologic age is the main criterion for considering orthotopic substitution in this patient group [22,23].

As a result of material prosperity and economic wealth, the prevalence of obese patients undergoing cystectomy and urinary diversion is steadily increasing in Western countries [24]. In fact, an obese patient may be a good candidate for an orthotopic bladder substitution as well as an abdominal continent or incontinent diversion. Potential difficulties in obese patients with cutaneous noncontinent and continent diversions are the manual application of a urostomy in daily use, self-catheterization of a continent reservoir through a thick abdominal wall, and bulky mesenteric attachments that may limit mobility and the ability to manipulate the pouch [25].

Life expectancy is an important factor when considering an orthotopic diversion. The primary aim of radical cystectomy should always be cancer control. However, extravesical and lymph node-positive disease are *not* necessarily exclusion criteria for performing an ileal neobladder [26]. Several studies have shown that the risk of urethral recurrence in these patients is low, ranging from 1.1% to 2.5% [20,27]. Neobladder construction *must not* be performed in patients with tumor at the urethral margin because the risk of urethral tumor recurrence would then be considerably high [19,27]. Moreover, with regard to extensive training and rehabilitation, some older patients may be better served with a simpler type of urinary diversion. In addition, physical and mental impairments that would preclude the ability to catheterize a neobladder, if necessary, should be ruled out in the preoperative setting: In some series, the need for clean intermittent catheterization at 5 yr after orthotopic diversion has been reported in up to approximately 4–10% of male patients and 15–40% of female patients [23,28,29].

A critical point in performing ileal neobladder is renal function. Metabolic disturbances as hyperchoremic acidosis and subsequent deterioration of renal function are due to the reabsorption of hydrogen acid through the ileal segment. Therefore, it is mandatory to evaluate renal function preoperatively and to exclude the possibility of prior renal deterioration secondary to tumor-related ureteral obstruction. In cases with postrenal obstruction, upper-tract deobstruction by percutaneous nephrostomy or ureteral stent sometimes allows better evaluation of the true renal function to preoperatively document minimally required renal function with a creatinine clearance of 60 ml/min [30]. Alternatively, the use of a gastric form of neobladder might be more appropriate in patients with renal impairment [11].

#### 4. Connecting the ureters to the ileal neobladder

##### 4.1. General considerations

Different techniques of valvular and nonvalvular ureteral implantation have been described in the literature. In contrast with continent cutaneous reservoirs and uretero-sigmoidostomies, which represent high-pressure, nonsterile systems needing a valvular antireflux ureteral implantation to protect the upper tracts, there are still controversies regarding the type of antireflux mechanism in low-pressure orthotopic substitutes [30].

Arguments for the incorporation of a valvular antireflux mechanism in orthotopic neobladders include the high percentage of bacteria in ileal reservoirs [31] and a valvular antirefluxive protection of the upper urinary tract in the native bladder. Because there is an increasing risk of intermittent catheterization over the long term in patients with neobladders [23,29,32], and this in turn promotes bacterial colonization, some form of antireflux mechanism might be necessary. Even though ileal neobladders are thought to be low-pressure reservoirs, urodynamic studies in Kock-type ileal pouches have demonstrated that the

intraluminal pressure is low (mean: 33 cm H<sub>2</sub>O) during storing but may increase significantly during voiding, reaching up to 77–150 cm H<sub>2</sub>O [33].

It has been shown that upper-tract deterioration may not become clinically apparent until 10–20 yr after orthotopic diversion and can occur despite radiographically unobstructed upper tracts. Moreover, many valvular antireflux methods are technically challenging and are flawed by considerable complications such as ureteroenteric stricture or nipple stenosis in approximately 3–10% of the patients with subsequent upper-tract deterioration [22,28,34]. A nonvalvular afferent isoperistaltic ileal segment of at least 20 cm, as proposed by Studer et al, has been demonstrated to prevent reflux by transmission of intra-abdominal pressure onto the afferent ileal segment during Valsalva maneuver [35]. A randomized prospective trial evaluating functional outcomes between Studer ileal pouch and the T-pouch is ongoing, and results are expected within the next few years [36].

Currently, there is no compelling evidence of whether a nonvalvular isoperistaltic ileal segment or valvular (eg, subserosal, nipple) ureteral implantation will provide better long-term protection of the upper urinary tract [2]. A brief overview of the different valvular and nonvalvular ureteral implantation techniques follows.

##### 4.2. Le Duc technique

One of the first valvular implantation techniques described by Le Duc consisted of the construction of an ileal sheet in which the ureter was implanted and introduced into the lumen of the reservoir via a transmural nonrefluxing channel and left unfixed intraluminally. In the modified technique, the distal ureteral end was widely spatulated, forming a ureteral plate, and directly adapted to the ileal mucosa [1,37].

##### 4.3. Nipple ureter

Another antireflux implantation technique is the nipple ureteral implantation with a split cuff described by Sagalowsky [38]. The ureter is spatulated approximately 1 cm and folded back to form a split-cuff nipple. The corners are sewn to each other except for a small gap proximally to prevent constriction.

##### 4.4. Kock ileal valve

The Kock nipple antireflux technique uses an ileal segment as an antireflux mechanism to create an intussuscepted ileal valve [39]. To fix the valve, four rows of staples affixed within the leaves of the valve and on the back wall outside the reservoir were used (Fig. 4; see section 5.1.2).

##### 4.5. Tapered ileal segment (T-pouch)

As an alternative technique, a tapered subserosal ileal segment that prolongs the conjoined ureters can be used and has been described by Stein et al. [28] (see section 5.1.2).



Fig. 4 – Valvular antireflux ureteral implantation using intussuscepted ileal segment (nipple valve).

4.6. Serous-lined extramural tunnel

A simpler form of an antireflux mechanism can be obtained by placing the ureters directly into serous-lined extramural tunnels [26] (see section 5.2.2).

4.7. Nonvalvular isoperistaltic ileal segment (“Studer technique”)

As a nonvalvular antirefluxive technique an afferent isoperistaltic ileal segment of at least 20 cm in length is used as an ileal chimney for antegrade urinary transport [35,40] (Fig. 5; see section 5.1.1).

5. Different techniques for ileal orthotopic substitution

Many forms of ileal neobladder construction have been described using different portions of bowel with different approaches in the connection and protection of the upper urinary tract [1,22,26,28,32,35,36,39]. To provide a meaningful overview for the recipient, we will focus on some techniques with long-term follow-up and a significant number of patients. The functional long-terms results of

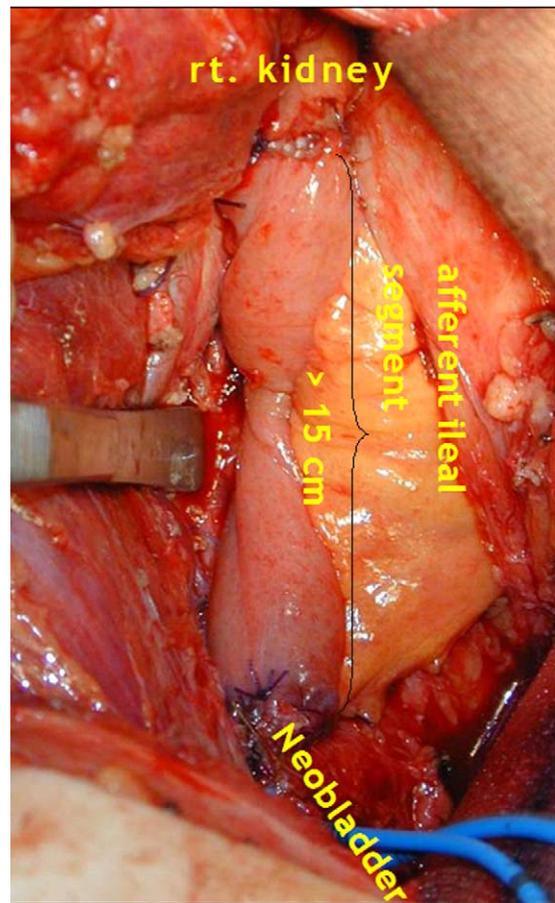


Fig. 5 – Antireflux mechanism using afferent ileal segment.

each type of diversion are given in Table 1. A schematic overview is given in Fig. 1.

5.1. Orthotopic substitution on a U-shaped and cross-folded reservoir (“Goodwin principle”)

5.1.1. Studer ileal neobladder

The Studer neobladder uses a 60- to 65-cm segment of terminal ileum that is dissected approximately 20–25 cm proximal to the ileocecal valve. After restoration of bowel continuity and closing of the mesenteric traps, the distal 40- to 45-cm segment is opened antimesenterically and serves as the reservoir, whereas the proximal 20- to 25-cm ileal segment remains intact and serves for ureteral implantation and prevention of reflux by isoperistaltic waves

Table 1 – Functional long-term results of most frequently performed types of ileal neobladder

Author	No. of patients	Median age, yr	Median follow-up, mo	Daytime continence, %	Nighttime continence, %	Need for CIC, %	Ureteroileal stenosis, %	Reflux, %
Studer et al. [40]	482	65	32	92	79	7	2.7	n.m.
Hautmann et al. [43]	383	63	57	95.9	95	5.6	9.3	3.3
Abol-Eneim et al. [26]	450	65	35	93.3	80	2	3.8	3
Stein et al. [28]	209	69	33	87	72	25	10	10

CIC = clean intermittent catheterization; n.m. = not mentioned.

(Fig. 5). Then the posterior plate of the U-shaped reservoir is formed by attaching the medial limbs by a running suture. The proximal end of the afferent intact segment is closed, and, after spatulating and stenting the ureters, the ureterointestinal anastomosis is performed separately for both ureters with an end-to-side technique at the proximal end (“Nesbit technique”). Before complete closure of the lateral borders of the reservoir, a separate buttonhole is created at the most caudal point of the pouch, and the urethroileal anastomosis is performed. Finally, the reservoir is closed completely [40]. This type of diversion has become one of the most popular forms of orthotopic diversion.

#### 5.1.2. The orthotopic Kock ileal pouch

The Kock ileal reservoir was first used as a continent cutaneous reservoir incorporating two intussuscepted nipple valves for both antireflux and continence mechanism. Later on, it evolved into an orthotopic substitute in which the afferent intussuscepted limb connected to the ureters was maintained to prevent reflux into the upper tracts. In brief, after antimesenteric incision, two approximately 22-cm distal ileal segments are placed in U-form to create the pouch whereas an approximately 17-cm ileal segment is used to create an intussuscepted 5- to 7-cm ileal valve. The valve is fixed with four rows of staples affixed within the leaves of the valve and on the back wall outside the reservoir [39]. The technical difficulties of achieving a durable and effective antireflux system and the risk of stone formation on the exposed staples as well as stenoses due to compromised vascularization of the valve have led many surgeons to develop novel constructions for antireflux mechanisms such as the serous-lined extramural tunnel and T-pouch ileal neobladder [26,28].

#### 5.1.3. The T-pouch ileal neobladder

In 1998, Stein reported the T-pouch neobladder as an alternative antirefluxive technique that inherits the same spherical configuration as the Kock ileal neobladder; the only difference is the use of an afferent ileal segment instead of an intussuscepted ileal valve as an antireflux system (“T-limb”). To ensure proper vascularization of the 3–4 cm of the distal part of the afferent ileal segment that forms the antireflux mechanism, mesentery windows (“Windows of Deaver”) are opened and Penrose drains are placed into each window. Then a series of sutures are passed through these windows consecutively to anchor the afferent ileal segment to the serosa of the two approximately 22-cm cephalad ileal segments of the reservoir. The afferent limb is tapered, and the two ileal segments are opened adjacent to the mesentery beginning from the cone end upward to the orifice of the afferent segment. The incision is conducted laterally to the antimesenteric edge and carried upward. This way, two ileal flaps are formed and placed onto the afferent ileal segment, thereby creating the antireflux mechanism [28].

#### 5.1.4. The Padua ileal neobladder (“vesica ileale Padovana”)

A 40-cm segment of terminal ileum is opened entirely at the antimesenteric border and reconfigured in a circular

manner (Fig. 1). A lower funnel of approximately 5 cm is created by means of two running sutures at the anterior and posterior sites to facilitate urethroileal anastomosis. Then the proximal loop is folded in a reverse S-shape, and the inner opposite borders are sutured to create an ileal cup. The ureters are implanted via two serous-lined intestinal troughs according to Abol-Eneim and Ghoneim [26]. Finally, the closure of the reservoir is completed at the anterior aspect by folding downward the upper edge of the ileal cup to obtain a spherical reservoir [41].

#### 5.1.5. Conjoined subserosal ureteral implantation in a cross-folded ileal reservoir (“I-pouch”)

This technique uses only approximately 40 cm of terminal ileum for the pouch. Basically, a Goodwin pouch is formed with a U-shaped ileal plate (length of each limb: 20 cm) that is cross-folded. The spatulated and conjoined ureters (“Wallace technique”) are placed in a subserosal trough of approximately 8 cm length at the upper end of the U-ileal plate. The reservoir has the same configuration as the Studer, Hemi-Kock, or T-pouch. The pouch is attached to the urethral stump either via a separate opening (female patients) or by leaving a small opening in the suture line closing the cross-folding (male patients). The differences are that the length of ileum used is reduced to 40 cm and that the directly implanted ureters lie on the dorsal wall of the pouch (Fig. 6). This facilitates an instrumentation of the upper tract at a later point [42]. The term *I-pouch* is derived from the fact that, contrary to the T-pouch, both conjoined ureters are directly implanted in a vertical straight line into the pouch.

## 5.2. W- or M-ileal reconfiguration

#### 5.2.1. Hautmann ileal neobladder

The Hautmann ileal neobladder is a W-configured spherical reservoir using approximately 70 cm of distal ileum that is intended to provide improved nighttime continence by large capacity. The entire segment is opened antimesenterically except for a 5-cm ileal segment flap that most easily reaches the urethra where the incision is carried out in the direction of the anterior mesenteric border to create a U-shaped form.

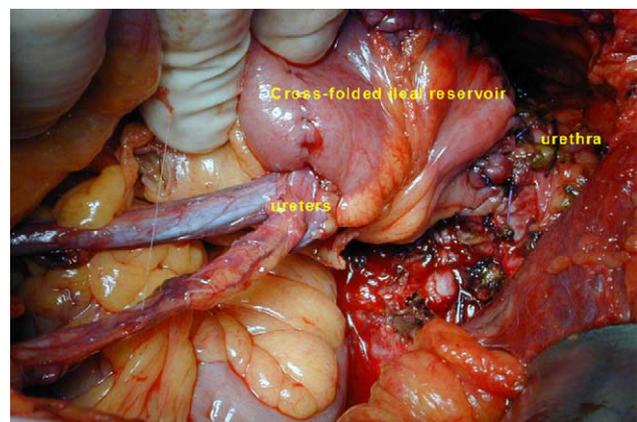


Fig. 6 – Conjoined subserosal ureteral implantation in a cross-folded ileal reservoir.

The four limbs of the detubularized bowel are closed with a running suture. The urethrointestinal anastomosis is carried out from inside the neobladder after excision of a buttonhole at the aforementioned U-shaped ileal segment. Then the ureters are implanted refluxively. Finally, the anterior wall is closed [43]. With regard to the length of ileal segment used to create a large capacity for improved nighttime incontinence, one has to bear in mind that metabolic disorders may more likely occur in this type of diversion than in others.

#### 5.2.2. *W-reservoir with serous-lined extramural tunnel*

In 2001, Abol-Enein and Ghoneim published the serous-lined extramural tunnel technique for ureteral implantation in a W-shaped ileal neobladder as an effective technique for preventing reflux [26]. In detail, an approximately 60-cm ileal segment is disconnected and opened entirely at the antimesenteric border. The medial limbs are closed with a running suture, whereas the two lateral flaps are joined by a seromuscular running suture to create the two serous-lined intestinal troughs. The spatulated ureters are stented and anastomosed to the intestinal mucosa. Then the tunnel is closed over the ureters, thereby forming an antireflux mechanism. At last, the anterior wall is closed side to side with a running suture, and the pouch is anastomosed at the urethra after defining and opening the most caudal point. According to Abol-Enein and Ghoneim, the serous-lined implantation technique provides several advantages. First, the ureters are protected from exposure to urine, allowing for improved wound healing and reduced risk of scarring. In addition, an especially long segment of ileum is not needed to create an antirefluxive system, like in T-pouch neobladders [28], and therefore is less demanding technically [44].

## 6. Risks and outcome of orthotopic neobladder construction in cancer patients

Neobladder reconstruction is a time-consuming and technically demanding procedure but inherits important advantages like improved body image, sexual function, and continence [45]. Therefore, Hautmann et al evaluated whether the willingness of the surgeon to offer an orthotopic diversion and the desire of the patient to undergo neobladder construction may lead to earlier performance of cystectomy and result in improved cancer-related outcomes [46]. In this respect, recent studies suggest that a delay in radical cystectomy for 3 mo may decrease cancer-specific survival [47]. Hautmann et al found that the mean time interval between primary diagnosis and cystectomy was significantly longer in conduit patients than in neobladder patients. Additionally, the 5-yr survival rates were significantly lower in conduit patients adjusted for all stages, suggesting that the availability of performing neobladder substitution may decrease the reluctance of both the surgeon and the patient to undergo radical cystectomy [46]. In female patients, there is evidence now that using an orthotopic neobladder after cancer-related cystectomy does not compromise

oncologic outcome as long as we adhere to predefined anatomic and functional pathologic guidelines [6,48].

The difficulties of the interpretation and deduction of meaningful findings of quality-of-life (QoL) studies for clinical practice are demonstrated in a systemic review by Porter and Penson, performing a review of a total of 378 studies [49]. Based on their inclusion criteria (adult patients, bladder cancer, comparative studies, original research, primary study outcome related to QoL, use of defined QoL instruments), only 15 of these 378 studies were appropriate for analysis. Moreover, none of the 15 studies was randomized. Only one study was prospective. Only two-thirds used validated QoL instruments, and only 73% used bladder cancer disease-specific instruments. Therefore, the authors concluded that the current body of evidence was insufficient to provide meaningful conclusions to the question of whether any type of diversion is superior to another on the basis of health-related QoL outcomes.

## 7. Conclusions

Orthotopic neobladder substitution is now considered the diversion of choice for the majority of patients, both male and female, undergoing radical cystectomy and is the procedure with which all other types of diversion must be compared. A comprehensible discussion with the patient about all options for urinary diversion as well as the potential short- and long-term risks and the beneficial effects of each type of diversion is mandatory for improved postoperative compliance and functional outcomes. Intraoperative frozen section analysis of the distal urethral margin is necessary to reduce the risk of recurrence.

All types of neobladder construction are based on the concept of detubularization and folding to provide a low-pressure reservoir. In this respect, there is substantial agreement in the literature that the terminal ileum possesses superior anatomic and functional characteristics. Given the lack of prospective randomized trials, controversies still exist with regard to the technique of preventing reflux in orthotopic substitutes and the superiority of one neobladder technique over others, provided the detubularized intestinal segment is reconfigured to an adequate-sized spherical reservoir.

## Conflicts of interest

The authors have nothing to disclose.

## Funding support

None.

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