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# Laparoscopic Radical Cystectomy with Ileal Orthotopic Neobladder for Bladder Cancer: Current Indications and Outcomes

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# Keywords

lleal orthotopic neobladder  $\cdot$  Radical cystectomy  $\cdot$  Bladder cancer  $\cdot$  Intracorporeal urinary  $\cdot$  Diversion  $\cdot$  Postoperative complications

### **Abstract**

Background: Laparoscopic radical cystectomy (LRC) with ileal orthotopic neobladder (IONB) reconstruction is one of the most promising methods for bladder cancer treatment; its advantages include a small incision size, less blood loss, improved perioperative outcome and tumor prognosis, and a positive self-image postoperatively. The short-term benefits of various IONB reconstruction procedures reported thus far include a simple process, short operative time, less intraoperative bleeding, few postoperative complications, and good postoperative neobladder function; in the long term, these benefits engender good quality of life of the patients. Here, we explored and summarized the more novel and available IONB reconstruction procedures to identify the safest, most efficient, and simplest IONB reconstruction techniques for patients with bladder cancer. Summary: LRC with IONB reconstruction is technically feasible; however, most of the relevant studies have been short, employing a small sample size and a retrospective design. However, long-term, largescale, prospective studies identifying the most appropriate bowel segments for IONB reconstruction, comparing intracorporeal and extracorporeal IONB reconstruction, assessing currently available IONBs, and resolving relevant postoperative complications further, with a focus on patients with bladder cancer, are warranted. *Key Message:* Several procedures for LRC with IONB reconstruction have been reported thus far. However, there is no consensus regarding the IONB reconstruction procedures most beneficial to patients with bladder cancer. Our review may aid researchers in developing a simple, safe, and efficient LRC with IONB reconstruction procedure for patients with bladder cancer.

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## Introduction

Bladder cancer is the 10th most common form of cancer worldwide, responsible for approximately 3.0% of all new cancer diagnoses and 2.1% of all cancer deaths [1, 2]. Bladder cancer mortality is mainly determined based on the pathologic stage. Approximately 25% of newly

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Table 1. Benefits and complications of ONBs with different intestinal segments

Intestinal segment used	Benefits	Complications
llium or ileocecum	More compliant and less contractile than the colon and stomach	Hypokalemic hyperchloremic metabolic acidosis Fat and bile-salt malabsorption Diarrhea Vitamin B12 deficiency Bone demineralization
Colon	ldeal for patients with a history of pelvic radiotherapy	Hypokalemic hyperchloremic metabolic acidosis Increased mucous production Bone demineralization Pyelonephritis Adenocarcinoma risk at anastomosis
Jejunum	Ideal for patients with a history of pelvic radiotherapy	Hyperkalemic hyperchloremic metabolic acidosis Nausea or vomiting
Stomach	Ideal for patients with a history of pelvic radiotherapy and low mucous production, as well as those with renal dysfunction, liver dysfunction, or both	Hypokalemic hyperchloremic metabolic alkalosis Hematuria-dysuria syndrome

diagnosed bladder cancers are muscle-invasive [3]. Radical cystectomy (RC) with pelvic lymph node dissection is the gold standard treatment for high-grade muscle-invasive bladder cancer [4, 5].

With the development of newer laparoscopic instruments and surgical techniques, laparoscopic RC (LRC) has become highly feasible and safe, with numerous benefits. A recent series of randomized controlled trials demonstrated that compared with open surgery, LRC is associated with smaller incisions, less blood loss, and better perioperative outcomes, all with comparable cancer prognosis [6, 7].

Ileal orthotopic neobladders (IONBs) simulate a part of the normal physiological urination process. With IONBs, patients do not need to wear a urine collection bag after a radical resection; they alleviate the psychological impact related to wearing a urine collection bag and aid the patients in resuming their social activities postoperatively.

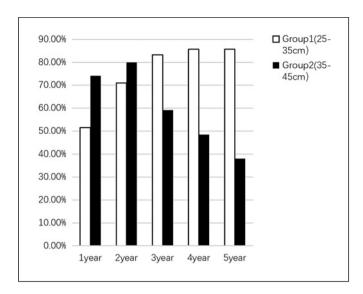
In this review, we discuss the potential and challenges of bladder LRC with IONB for urinary diversion. We also focus on various orthotopic neobladder (ONB) procedures after LRC, including their origin, creation, benefits, and limitations, as well as the common complications, clinical feasibility and safety, and limitations of LRC with IONB. Finally, we discuss the future research directions for LRC with IONB.

## **Clinical Progression after LRC with IONB**

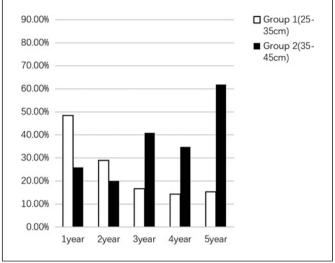
Surgeons are constantly exploring superior forms of urinary diversion in patients with bladder cancer. Bricker et al. [8] reported the use of an ileal conduit for the first time in 1950, and it remains the most commonly used form of urinary diversion worldwide. Patients with an ileal conduit require lifelong stoma use or self-catheterization. In contrast, LRC with an ONB is a high-quality option that aids patients in improving their postoperative self-image and quality of life.

## Intestinal Segments for ONB Reconstruction

An ideal intestinal bladder substitute should demonstrate low pressure, adequate capacity, and high compliance to provide continence and voluntary control of voiding without residual urine [9]. Urologists have attempted to use the stomach and jejunum as materials for neobladder reconstruction; however, these options have been demonstrated to be unfeasible. At present, the ileum is the most favored bowel segment for neobladder reconstruction, followed by the ileocecal cecum and the colon [10]. Table 1 summarizes the benefits and complications of ONBs with different bowel segments [11]. Accumulating evidence has confirmed the safety and feasibility of IONB. For instance, a meta-analysis and a



**Fig. 1.** Statistical chart of good postoperative urinary tract control after 5 years of follow-up.



**Fig. 2.** Statistical chart of poor postoperative urinary tract control after 5 years of follow-up.

clinical observation study have reported that IONB improves patients' physical function and self-image postoperatively [12].

Zheng et al. [9] assessed the feasibility of using a shorter (25–35 cm) and longer (35–45 cm) ileum segment as an IONB material in observation groups 1 and 2, respectively. The authors noted that the IONB composed of the longer segment expanded rapidly over time, resulting in urinary incontinence. The mean maximum urine flow rates 5 years postoperatively were 19.0  $\pm$  2.3 and 14.2 ± 3.5 mL/s in observation groups 1 and 2, respectively. Follow-up was mainly based on the number of changing pads to assess the patient's urinary tract control (postoperative criteria for good urinary tract control: the number of pads used per day was less than or equal to 1, and the number of pads used was >1 for poor urinary tract control). From 1 to 2 years after surgery, the rate of good urinary tract control was consistently lower in observation group 1 than in observation group 2, and the rate of poor urinary tract control was consistently higher in observation group 1 than in observation group 2. However, from 3 to 5 years after surgery, the rate of good urinary tract control began to be consistently higher in observation group 1 than in observation group 2, and the rate of poor urinary tract control was consistently lower in observation group 1 than in observation group 2 (Fig. 1, 2). These follow-up data confirmed that IONBs composed of a 25-35-cm-long ileum maintain good bladder function for a longer period than IONBs composed of a 35-45-cm-long ileum.

Although the ileum is the preferred material for ONB reconstruction, it may be inapplicable to some patients. Compared with that of other intestinal segments, the natural anatomical position of the sigmoid colon - at the back of the pelvis and the peritoneum - makes it more conducive for ureteral rearrangement and urethral anastomosis. Moreover, the thickness of the sigmoid colon wall is larger than that of other intestinal segments, preventing its overexpansion over a long period. Furthermore, because its diameter is large, relatively short sigmoid colon segments are required for ONB creation. The sigmoid colon mucosa only absorbs water, sodium, and chloride. Therefore, in contrast to IONBs, sigmoid colon ONB does not cause vitamin B12 deficiency and thus leads to fewer metabolic complications. Therefore, Nicita et al. [13] retrospectively analyzed 144 patients with sigmoid colon ONBs. At the 5-year follow-up, the daytime and complete incontinence rates were 36% and 45.3%, respectively, with a maximum bladder capacity of 433 mL; moreover, the results of other urodynamic assessments were good. The authors suggested that sigmoid colon ONBs demonstrate an increased sense of filling, low diastolic tendency, low incontinence rate, negligible metabolic imbalance, and few adverse effects on the upper urinary tract function. However, many patients are lost to follow-up over time, particularly when they achieve good ONB control. Therefore, further research on the clinical efficacy of sigmoid colon ONBs is warranted.

ONB Reconstruction Procedures

Open RC versus LRC

Open RC (ORC) is one of the most invasive urological surgical procedures; nevertheless, it remains the most commonly used procedure in clinical practice. Parra et al. [14] reported laparoscopic total cystectomy for the first time in 1992. Laparoscopy instruments provide a clear surgical view, aiding surgeons in identifying tissues and blood vessels and performing thorough manipulation. Considering that it only slightly interferes with the bowel, laparoscopic surgery has become a crucial bladder cancer treatment tool.

Liu et al. [15] compared the clinical efficacy and safety of laparoscopic surgery (n = 48) with those of open surgery (n = 39). Their results indicated that compared with open surgery, laparoscopic surgery led to a significantly lower perioperative bowel obstruction rate, less intraoperative bleeding and postoperative pain, and substantially shorter gastrointestinal function recovery time and postoperative hospital stay [15]. In contrast, Tostivint et al. [16] demonstrated that in the long term, laparoscopic surgery resulted in a higher rate of ureteroileal stenosis than open surgery; however, the authors noted no differences in functional outcomes or long-term quality of life between the two ONB reconstruction approaches.

Similarly, Simone et al. [6] compared intracorporeal procedures (n=64) and open procedures (n=299) through Kaplan-Meier analysis. Both the groups demonstrated comparable disease-free, cancer-specific, and overall survival, with a similar mean lymph node yield (33.4 for intracorporeal procedures and 31.4 for open procedures) and a positive margin incidence (<1%). However, the total perioperative complication rate was higher in the open group than in the intracorporeal group (91.3% vs. 42.2%) [6]. These data confirmed that intracorporeal surgery is an oncologically sound surgical procedure; however, its long-term oncological outcomes warrant further improvement.

In general, LRC with ONB is safe and feasible. However, surgeons must assess their patients' clinical situation before choosing between LRC and ORC. Furthermore, whether LRC can provide superior clinical outcomes to those of ORC requires further validation.

Intracorporeal ONB Reconstruction versus Extracorporeal ONB Reconstruction

The pelvic lymph node dissection outcomes of intracorporeal and extracorporeal ONB reconstruction demonstrate no significant differences. However, the bladder is located deep within the human pelvis and thus provides a small surgical space; therefore, some surgeons believe that during ONB reconstruction, this small surgical space may engender limitations such as increased bleeding and complication rates. In contrast, some surgeons believe that extracorporeal ONB reconstruction may expose the bowel to air for a longer period than favorable. It may also increase the risk of traction on the gastrointestinal tract tissues, as well as that of some other postoperative complications.

Zhao et al. [17] compared modified intracorporeal and extracorporeal ONB reconstruction techniques and found that both led to low late complication rates and good functional outcomes, all without worsening the tumor prognosis. Nevertheless, although the time required for suturing the pouch was considerably shorter for extracorporeal ONB reconstruction than for intracorporeal ONB reconstruction, the total mean operative time demonstrated no significant differences [17].

IONB Types

In clinical practice, many IONB types are available; of these, the Studer and Hautmann IONBs are the most popular among urologists. However, Studer and Hautmann IONB reconstruction can be complex, with long operative times and high blood loss. Many types of modified IONB reconstruction methods have been reported. However, considering the high technical complexity and the long operative time typically required for IONB reconstruction, the pace at which newer intracorporeal IONB reconstruction methods are developed has been slow. Moreover, surgeons have yet to reach a consensus regarding the most appropriate IONB reconstruction method. Nevertheless, urologists are continually developing and improving the IONB reconstruction method to meet their patients' physiological needs by using a simplified procedure (Table 2, comparison of different ONB types).

Bianchi et al. [18] retained the advantages and improved on the limitations of the pyramidal neobladder, Gaston's Y-shaped neobladder, and Koie's neobladder reconstruction techniques by using a unique craniocaudal running suture to form the neobladder's posterior wall. Next, the authors used two-directional sutures to reconfigure the anterior wall, creating a spherical shape. Finally, they anastomosed the ureter to the posterior wall of the neobladder to form a modified detached papilla with separate sutures without using an additional antireflux technique (Fig. 3) [18]. The resulting "Shell" neobladder can maintain its spherical shape, reducing its intracavitary pressure. "Shell" neobladder reconstruction requires a few sutures in various directions, making it

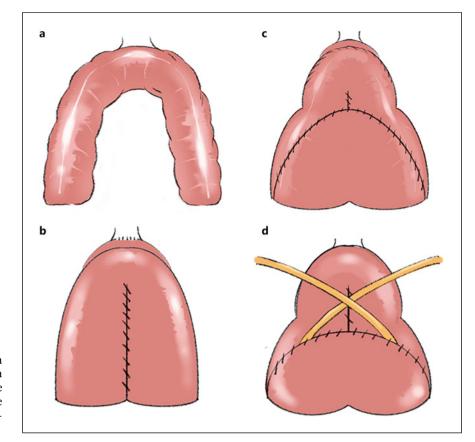
Table 2. Comparison of different ONB types

	Gut segment used	Segment length	Median NB volume, mL		Median operative time, min	Median estimated blood loss, mL	Type of surgery
"Shell" neobladder (12 months after surgery, $n = 30$ )	lleum	40 cm	-	Daytime continence: 73.3% Nighttime continence: 60%	493	400	Robot-assisted surgery + intracorporeal constructs
"IUPU" neobladder (12 months after surgery, n = 17)	lleum	54 cm	478	Daytime continence: 100% Nighttime continence: 88.2%	248	150	Laparoscopic surgery + extracorporeal constructs
Xing's neobladder (12 months after surgery, $n = 38$ )	lleum	60 cm	400	Daytime continence: 94.7% Nighttime continence: 81.6%	330	328	Laparoscopic surgery + intracorporeal constructs
"VON" (3 months after surgery, $n=6$ )	lleum	36 cm	272.5	Daytime continence: 67% Nighttime continence: 50%	273	237	Laparoscopic surgery + intracorporeal constructs
Nicita's neobladder (5 years after surgery, n = 75)	Sigmoid	20~25 cm	433	Daytime continence: 36% Complete continence: 45.3%	-	-	Open surgery
Frog neobladder (1 year after surgery, n = 120)	lleum	60 cm	398	Daytime continence: 92% Nighttime continence: 82%	280	-	Open surgery

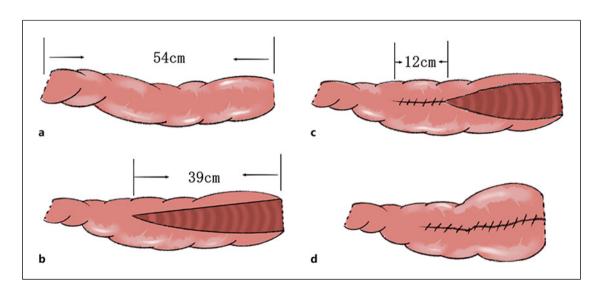
easier than the Studer neobladder reconstruction. "Shell" neobladders are formed entirely within the intracorporeal cavity and have the advantage of shorter operative times, less bleeding, lower rates of early and late complications, and lower rates of day and night incontinence, based on data collected from short-term clinical observations. However, no urodynamic data demonstrating whether the "Shell" neobladder reaches a sufficient volume with low internal pressure (to protect the upper urinary tract), as well as long-term data indicating the postoperative benefits of the shell neobladder, are unavailable.

Hong et al. [19] created the Institute of Urology Peking University (IUPU) neobladder based on Studer's report.

The authors used a 54-cm-long segment of the ileum to create a pouch and an afferent limb. The pouch comprised an ileum segment that was completely detubulated; here, detubulation eliminated peristaltic-induced pressure waves and provided the maximum volume and minimum surface area of the ileum. The pouch was constructed by simply folding the ileum twice, adjusting the orientation of the ileal segment, and then suturing two parallel pairs of edges (Fig. 4). IUPU neobladder reconstruction requires a relatively short piece of the ileum used and involves a relatively simple procedure; both of these factors reduce the time and difficulty of the process. Hong et al. [19] assessed the pathological findings of their



**Fig. 3.** Surgical procedures for the construction of "Shell" neobladder. **a** Anastomosis between the urethra and the ileal tract identified for the future neobladder. **b** Configuration of the posterior plate. **c** Ureteral-neobladder anastomoses. **d** Configuration of the anterior plate.



**Fig. 4.** Surgical procedures for the construction of IUPU neobladder. **a** Take a 54-cm section of ileum. **b** The distal 39 cm of the ileum was detubularized along the antimesenteric border and folded at the mark points. **c** First fold of the distal ileal segment with the two 12-cm segments sutured together. **d** Second fold, forming the posterior wall of the neobladder and closing the anterior wall of the neobladder.

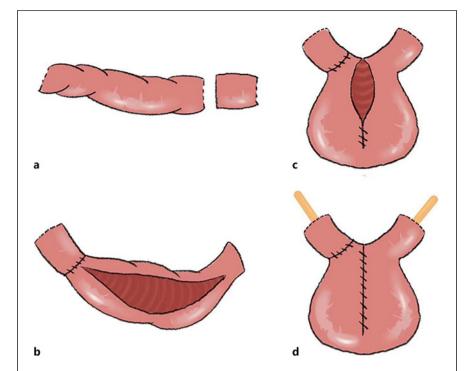


Fig. 5. Surgical procedures for the construction of Xing's neobladder. a A 60-cm ileum from approximately 25 cm proximal to the ileum was taken, and 10 cm of proximal ileum was excised. b The excised proximal 10 cm of ileum was flipped to the right and anastomosed to the distal bowel, leaving a segment of bowel of equal distance distally and to the left to complete the bilateral pass to the isoperistaltic limb, and the remaining bowel in the center was broken off and detubulated. c, d The anterior and posterior walls of the neobladder were sutured, and the ureter was anastomosed.

patients with an IUPU neobladder over a median follow-up of 22.5 months. During the follow-up period, only two cases demonstrated recurrence, whereas only one case demonstrated metastasis. After 12 months postoperatively, the daytime and nocturnal incontinence rates were 100% and 88.2%, respectively. The median neobladder volume, residual volume, and maximum flow rate were 478 mL, 0.0 mL, and 18.9 mL/s, respectively [17]. In general, the IUPU neobladder reconstruction is a highly simplified procedure with minimal difficulty, leading to relatively few late complications but good functional outcomes without a worsened cancer prognosis.

The neobladder created by Xing et al. [20] produced favorable results in the clinical practice. It was constructed using a 60-cm-long ileal segment, isolated approximately 25 cm proximally to the ileocecum. The proximal 20 cm of the ileal segment was divided into two 10-cm-long parts for bilateral isoperistaltic afferent limbs. The proximal 10-cm-long part was moved to the distal end of the ileal segment to form the right isoperistaltic afferent limb, whereas the remaining proximal 10-cm-long ileal segment was retained to form the left isoperistaltic afferent limb. The remaining 40-cm-long ileal segment was detubulated along its antimesenteric border to create a reservoir. The resulting neobladder was sutured to achieve a spherical shape (Fig. 5). Notably, this procedure was performed entirely in intracorporeal. Moreover, the total operative

time and postoperative urinary diversion time decreased significantly over the 20 repetitions of the procedure. The reduction in the operative time confirmed not only the increased proficiency of the operating surgeon but also the ease of the procedure. Finally, this procedure was associated with a low grade 1 or 2 complication rate and good functional outcome at 90 days postoperatively, without worsening cancer prognosis [17].

The Vesuvian Orthotopic Neobladder (VON) technique was created by Del Biondo et al. [21] on the basis of the Y technique; the authors used a 36-cm-long ileum segment for neobladder reconstruction and ipsilaterally anastomosed both the ureters with complete detachment within the two horns (Fig. 6). Among all ONB reconstruction techniques reported to date, VON reconstruction requires the shortest ileal segment; this allows the ureters to remain in their natural anatomical position, considerably reducing the risk of ischemia. Moreover, the use of sutures during the procedure largely reduces the operative time (mean total operative time =  $273.3 \pm 18.6$ min; mean time for neobladder reconstruction =  $63.7 \pm$ 16.1 min) [21]. However, VON's nonspherical shape reduces its volume to levels lower than those of other IONBs (mean bladder at 3 months postoperatively =  $272.5 \pm 17.1$  mL). In other words, in terms of short-term results, VON outcomes are not significantly superior to those of other IONB techniques.

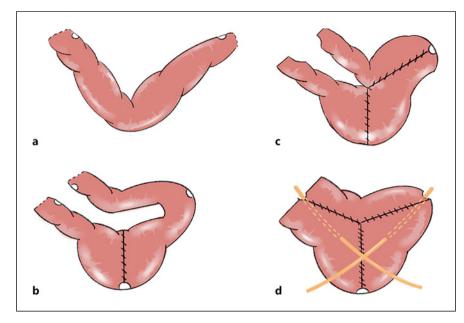


Fig. 6. Surgical procedures for the construction of VON. a Take a 36-cm-long segment of ileum. b, c A 60-mm stapler is introduced through the first incision to make the caudal horn, followed by a second 60-mm stapler through the second incision for the left horn. d After removal of the central part of the metal suture exceeding the intestinal resection, the afferent and efferent stumps are sutured together with a 60-mm mechanical stapler forming the right lateral horn; the ureter is placed on the same side of the horn, and then the ureteral catheter is reversed through the anterior wall of the neobladder.

Although many other technically feasible IONBs, such as FROG Neobladder [22], have been reported thus far, their reconstruction techniques have been assessed in small-scale, short-term, retrospective studies. Therefore, additional larger scale studies evaluating the outcomes of these techniques over a long period are needed.

## Challenges of LRC with IONB

Postoperative Complications of LRC with IONB Factors Leading to Postoperative Complications

RC is one of the most difficult urological procedures. It is associated with an extremely high postoperative complication rate, which increases the patients' length of hospital stay and total hospital cost, worsens their physical recovery and quality of life, and reduces their postoperative survival. These postoperative complications may be related to several factors, such as age, sex, and surgical approach. However, clinical studies on this poor patient prognosis are lacking.

High glucose and low albumin can influence postoperative complications. The oxidative intermediates of glucose may convert to amino acids, which may then be used to synthesize proteins such as albumin. Cheng et al. [23] considered this glucose-albumin relationship and proposed a new postoperative complication index: the postoperative ratio of albumin to blood glucose, represented as A/G. Through multivariate logistic regression, the authors found that A/G is an independent factor associated with early complications. Its threshold is set at 3.65, with a specificity of 0.716 (true-negative rate) – which implies that a patient with A/G = 3.65 has a 71.6% probability of having no complications [23]. Therefore, A/G can be used to assess the early signs of postoperative complications; it may aid urologists in improving each patient's postoperative outcomes and recovery individually. Finally, intraoperative blood transfusions (rather than postoperative transfusions), hyperglycemia and diabetes mellitus [24–26], and obesity have all been identified as factors contributing to unfavorable postoperative recovery in RC patients [27].

Urinary Tract Infections and Ureteral Stricture

RC with urinary diversion significantly increases infection risks; the overall infection rate can range from 41% to 25% [28, 29]. Urinary tract infections (UTIs) are the most common infection types in patients who undergo RC with IONB. Moreover, postoperative infection treatment is associated with a significant increase in treatment costs. Among all oncological conditions, bladder cancer currently requires one of the most expensive treatments [27].

Mano et al. [30] reported that 29% of patients with neobladders and 8% of patients with ileal conduits developed UTIs in the first 3 postoperative months; in other words, compared with ileal conduits, neobladders significantly increased UTIs risks. Here, the most common pathogens were *Pseudomonas aeruginosa* and *Escherichia coli*. However, a series of urodynamic examinations up to

6 months after surgery revealed that the patients with neobladders demonstrated a significant increase in the maximum flow rate and bladder volume over time but a reduction in the residual urine volume and UTI rate. Moreover, atrophic changes in the neobladder's intestinal mucosa, which occur 3–6 months after surgery, may make it less susceptible to bacterial colonization or infection [31]. Finally, changes in pathogen recognition receptor expression patterns or innate immune activation may engender a decrease in the incidence of postoperative UTIs over time [32]. These results thus confirm that ONB patients demonstrate a gradual reduction in UTI incidence over time.

Currently, antibiotic administration is the most preferred method for UTI treatment and prevention. However, antibiotic resistance poses a significant challenge to clinicians. Gaplione et al. [33] proposed a novel antimicrobial strategy for the treatment of catheter-associated UTIs. The author combined human apolipoprotein B-derived antimicrobial peptides with conventional antibiotics and noted that the combination reduced the biofilm thickness and coverage synergistically [33].

A ureteroileal anastomotic stricture (UIAS) is one of the most common post-ONB complications. In their study, Benson et al. [34] noted a UIAS rate of 8.9% among patients who underwent ONB reconstruction. These UIASs resulted from perioperative and recurrent UTIs producing an inflammatory response, which hindered the healing of the new anastomosis and subsequently led to scarring and ulceration at the anastomosis [34]. Recurrent UTIs may create a similar environment around the anastomosis, leading to stricture development. In other words, UTIs are associated with UIAS development. Anastomotic techniques used for ONB reconstruction may also be associated with stricture development. A study reported that the stricture rate was the highest in patients with a dilated ureter preoperatively who underwent Le-Duc ureteroenteric anastomosis (35.54%) but the lowest incidence in patients with a nondilated ureter preoperatively who underwent Wallace ureteroenteric anastomosis (2.4%). Moreover, the stenosis rate is higher in the left ureter than in the right. In particular, during ureteroenteric anastomosis, the left ureter is moved across the sigmoid colon mesentery to reach the right side, which potentially increases ischemia and causes stenosis in the left ureter [34].

Numerous recent studies have focused on improving minimally invasive surgical techniques, specifically on the association of various surgical approaches with UIAS development. Parker et al. [29] found that none of the cystectomy types lead to the later development of UIASs; in particular, ORC leads to a nonsignificantly lower UIAS rate than LRC and robotic-assisted RC (both of which involve greater tissue traction and compression).

The UIAS etiology is complex; thus, it may be associated with factors other than UTIs, anastomotic techniques, and anti-reflux techniques. In most patients, UIASs are asymptomatic, but they are diagnosed through routine follow-up imaging. A method to prevent the UIASs involves reducing the risk of folding angle-associated stenosis by ensuring that the ureter is in its original anatomical position during ONB reconstruction. Moreover, opting for endoscopic or reconstructive ureteral ileal reimplantation over open surgery (depending on the length and caliber of the stenosis) can increase the effectiveness of UIAS treatment [29].

#### Intestinal Obstruction

Intestinal obstruction is one of the most common post-RC gastrointestinal complications caused by various factors, including unavoidable intraoperative bowel manipulation, prolonged postoperative fasting leading to electrolyte imbalance, and nutritional deficiencies. Hollenbeck et al. [35] evaluated 2,538 RC patients for risk factors for potentially avoidable complications during the postoperative period. Of them, 774 (30.5%) patients developed surgery-related complications, including intestinal obstruction (n = 247; 9.7%). This prolonged the patients' hospital stay and increased their medical costs.

The most common methods to prevent or treat intestinal obstruction after RC include bowel preparation with prophylactic antibiotics, controlled nasogastric catheter use, and surgery. Blackwell et al. [36] reported that the rate of admission for intestinal obstruction after RC increased over time. Nevertheless, patients who underwent surgical treatment within the first 4 days of admission led to a 43% and 45% decrease in the risk of minor-to-moderate and severe complications, respectively, as well as a 3.1-day reduction in the length of postoperative hospital stay. Therefore, early surgical interventions may improve post-RC intestinal obstruction outcomes.

Studies on preventing the development of intestinal obstruction, with a focus on directly reducing postoperative distress, have also been reported. Intraoperative manipulation may compromise the intracorporeal barrier and allow adhesions to occur; this may be prevented by creating a synthetic physical barrier separating the injured tissue surface from the adjacent organs. Hyaluronic acid (HA)/carboxymethylcellulose (CMC) is a sol-gel transition barrier used as a physical barrier; it is relatively more effective when covering injured surfaces. HA,

one of the main components of the extracellular matrix, is an anionic polysaccharide; it is found in the connective tissue, skin, cartilage, hyaline, and synovial membranes. CMC is also an anionic polysaccharide that is more hydrophilic than HA. In one study, HA/CMC drops were given to patients who received LRC and were followed continuously. None of these patients developed postoperative adhesive bowel obstruction and demonstrated nonsignificant differences in surgical or oncological outcomes or complications. However, long-term, largescale, randomized controlled trials confirming these findings are required [37]. In addition, chewing gum use after surgery, a safe and inexpensive method, may accelerate bowel function recovery by reducing the time to the first bowel movement, thus improving bowel function recovery and reducing bowel obstruction incidence [37, 38].

The bowel suspension technique (BST), described by Song et al. [39], prevents early intestinal obstruction. In this short and simple procedure, the right hemithorax and cecum are first moved into place after a U-shaped IONB is constructed, and then, intestinal continuity is restored with mechanical sutures; finally, the proximal mesentery of the anastomosed bowel is then sutured to the retroperitoneum to prevent the proximal mesentery from falling into the right pelvic cavity. The pelvic cavity becomes empty after RC; even after the sigmoid colon and IONB are manipulated to occupy the areas on the left side and middle of the pelvic cavity, the space on the right side may remain empty, increasing the risk of bowel protrusion on the right side of the pelvis. Nevertheless, with BST, the portion of the bowel anastomosis created using mechanical anastomosis does not fall into the pelvis, but it remains suspended above the pelvis; this prevents bowel protrusion, which can lead to intestinal obstruction. In one study, out of a total of 310 patients, 100 (32.3%) of 105 patients who received BST developed paralytic bowel obstruction and 15 (4.8%) developed early bowel obstruction. The incidence of postoperative bowel obstruction requiring surgical intervention was significantly lower in patients who received BST compared with those who did not (6.8% vs. 1.0%). In general, the BST was negatively associated with early bowel obstruction [39]. However, more data are needed to validate the clinical results of this technique.

Urinary incontinence is also one of the common complications. Especially for women, incontinence problems, mainly nocturnal incontinence, are a major predictor of negative impact on the quality of life of female patients undergoing ONB. Daytime and nocturnal incontinence have been reported to range from 60% to 90% and 26% to 92%, respectively, in female patients after

ONB. This suggests that a significant percentage of female patients will face incontinence after surgery [40]. It was suggested that this phenomenon may be related to the loss of the forced urinary sphincter mechanism and/or loss of sphincter tone at night as a result of surgery, and that the wall of the neobladder is stretched as tension increases during sleep. In addition, involuntary highamplitude contractions of the neobladder are secondary to bowel movements, and thus hyperfunction of the neobladder has also been suggested as a potential mechanism for the high incontinence rate, as reported in a urodynamic evaluation of 44 women in which 21 women (48%) had hyperfunction of the neobladder, and 7 women (16%) had low maximal urethral closure pressures and leak point pressures [41]. But the exact reasons remain controversial [42]. Techniques such as preserving nerves to improve control of the pelvic floor muscles [43] or using round ligaments to suspend the posterior wall of the neobladder to restore it to its original anatomy [44] have been invented by physicians in the hope of improving urinary incontinence, but the clinical data have shown no particular advantage for the time being. Studies have demonstrated that with time and postoperative exercise of the neobladder function pattern, most patients can maintain a low incontinence rate; however, their nocturnal incontinence rate may remain higher than their daytime incontinence rate [9, 20, 45]. For the complication of urinary incontinence, oxybutynin and verapamil [46], as well as tolterodine and mebeverine, may improve nocturnal incontinence with relatively few side effects [40, 46, 47].

## Promotion of LRC with IONB

Ileal conduit urinary diversion use increased significantly from 0% in 2005 to 95% in 2018; the highest increase was noted in intracorporeal ileal conduit use (from 0% in 2005 to 73% in 2018), whereas IONB use demonstrated a slight increase (from 0% in 2005 to 23% in 2018) [48]. Multiple factors may have resulted in low popularity of IONB reconstruction.

For practitioners, LRC with IONB remains complex and difficult. In particular, learning the entire procedure based only on the available reports and images can be difficult. However, because the number of IONB surgical procedures remains relatively small, the number of cases surgeons need to improve their surgical skills remains insufficient; this leads to the formation of a vicious circle.

Maurice et al. [49] reported socioeconomic status as an independent predictor of the urinary diversion type after RC. In high-volume hospitals, patients in the highest and second highest income groups were 4.5 and 3.3 times

more likely to select IONBs over ileal conduits, respectively. Similarly, at academic centers, the odds of the highest and second highest income groups selecting IONB were 3.2 and 2.1 times higher than those selecting ileal conduits, respectively. These observations were strongly associated with the costs related to the procedure and its postoperative complications. They may also reflect the influence of educational status on the choice between IONBs and ileal conduits; however, further research confirming this implication is warranted.

#### Conclusion

LRC with IONB requires a small incision; moreover, it leads to less blood loss and good perioperative results. In patients with bladder cancer, LRC with IONB does not affect cancer prognosis, but it facilitates near-normal urination; this improves the patients' quality of life and self-image. Therefore, it may be one of the most promising options for the surgical treatment of bladder cancer. However, comprehensive studies focused on identifying the bowel segments most appropriate for IONB reconstruction, comparing intracorporeal and extracorporeal IONB reconstruction, assessing currently available IONBs, and resolving relevant postoperative complications are required.

In this review, we discussed the potential of LRC with IONB as a surgical option for bladder cancer treatment, along with the related challenges and their potential solutions. Our observations may aid surgeons and urologists in creating a procedure for LRC with IONB reconstruction for patients with bladder cancer, which is simpler, safer, and more efficient than other available techniques.

#### **Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

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#### **Author Contributions**

L.G. and T.Z.: guideline development and manuscript editing; T.L.: manuscript revising; J.C.: project development and manuscript revising; H.G.: funding acquisition. All authors read and approved the final version of the manuscript.

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