

# Orthotopic neobladder reconstruction

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## Abstract

Orthotopic neobladder reconstruction is becoming an increasingly common urinary diversion following cystectomy for bladder cancer. This is in recognition of the potential benefits of neobladder surgery over creation of an ileal conduit related to quality of life (QoL), such as avoiding the need to form a stoma with its cosmetic, psychological and other potential complications. The PubMed database was searched using relevant search terms for articles published electronically between January 1994 and April 2014. Full-text articles in English or with English translation were assessed for relevance to the topic before being included in the review. Patients with neobladders have comparable or better post-operative sexual function than those with ileal conduits. They also have comparable QoL to those with ileal conduits. Orthotopic neobladder is a good alternative to ileal conduit in suitable patients who do not want a stoma and are motivated to comply with neobladder training. However, the selection of a neobladder as the urinary diversion of choice requires that patients have good renal and liver functions and are likely to be compliant with neobladder training. With benefits also come potential risks of neobladder formation. These include electrolyte abnormalities and nocturnal incontinence. This short review highlights current aspects of neobladder formation and its potential advantages.

**Key Words:** Erectile dysfunction, quality of life, urinary bladder, urinary diversion, urinary incontinence

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## INTRODUCTION

Bladder cancer (BC) is the ninth most common cancer worldwide. After prostate cancer, it is the second most common urologic malignancy worldwide. In both sexes, the age-standardized rate of BC in 2012 is 5.3/100,000 whereas the mortality rate stands at 1.9/100,000. The 5-year prevalence is 25.4/100,000.<sup>[1]</sup> BC is definitively diagnosed through histological examination of tissue samples that determines

the degree of cell differentiation (tumor grade) and spread (tumor stage). BC is staged using the tumor, node and metastasis system which considers the extent of local tumor spread (T), presence of cancer in lymph nodes (N) or metastasis (M). The “gold standard” treatment for high-grade BC is radical cystectomy with extended lymphadenectomy and urinary diversion, which includes ileal conduit, continent urinary reservoir and orthotopic neobladder. The type of urinary diversion performed [Figure 1] depends on the patient’s and surgeon’s preference, associated comorbidity and target quality of life (QoL) postoperatively. An orthotopic neobladder avoids the need to form a stoma and risk of stomal complications with associated physical and psychosocial effects; up to 63%, 58% and 42% of patients with an ileal conduit felt less complete, were apprehensive about stomal leakage and embarrassed due to the stoma, respectively.<sup>[2]</sup> However, there are other issues to consider with this orthotopic diversion such

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as patient suitability from a co-morbidity perspective as well as for compliance to a neobladder training regime, continence, sexual function and their anticipated QoL [Table I]. There are also some contraindications to orthotopic neobladder reconstruction such as renal and liver impairment, intestinal disease and cancer at the prostatic apex or bladder neck [Box 1]. The purpose of this review is to discuss the important considerations of orthotopic neobladder reconstruction, namely effects on electrolyte balance and nutrition, neobladder training and continence. The effect of this procedure on sexual function and QoL in comparison with ileal conduit urinary diversion are also discussed.

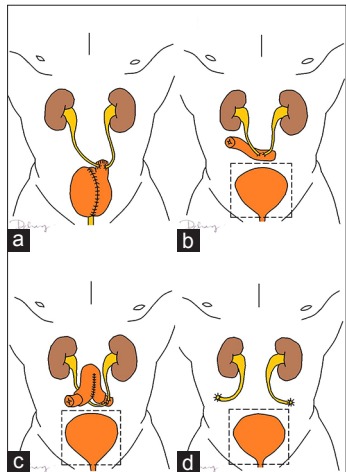
**LITERATURE REVIEW**

The PubMed database was searched using the following terms: “neobladder,” “orthotopic,” “urinary diversion,” “ileal conduit,” “BC,” “cystectomy,” “continence,” “QoL,” “urodynamics,”

“complication” and “sexual function” in various AND/OR combinations for articles published electronically between January 1994 and April 2014. All original full-text articles in English were assessed for relevance to the topic so that this review can present a balanced view of current research findings. There was no exclusion of articles based on the level of evidence as a significant portion of relevant articles were case series. Publications in other languages were also included only if there was an English translation of the article and the content supplied useful information. Furthermore, the reference lists of included articles were searched to include further relevant papers even though they may be published prior to year 1994.

**PROCEDURE/TYPES OF ORTHOTOPIC NEOBLADDER**

Although there are various ways of folding intestinal segments to construct a neobladder, each method has the aim of creating a spherical reservoir, the significance of which will be discussed below. Described types include Camey I and II (U-shaped), modified Camey II (Z-shaped), Kock (sagittally-folded U-shaped), T-pouch (sagittally-folded U-shaped), Studer (sagittally-folded U-shaped), Hautmann (W-shaped) and the Abol-Enein and Ghoneim modification of the W pouch,<sup>[3]</sup>



**Figure 1:** Types of urinary diversion surgery; (a) orthotopic neobladder (specifically Hautmann neobladder with chimney ureteroileal anastomosis), (b) ileal conduit, (c) continent ileostomy, and (d) cutaneous ureterostomy. Fenestrated box represents the removed native bladder. (Figure illustrated by Dwayne Chang. Copyright Nathan Lawrentschuk and Dwayne Chang. Reproduced with permission.)

**Box 1: Characteristics of patients who are not suitable to undergo orthotopic neobladder reconstruction**

- Chronic renal failure with serum creatinine  $\geq 150 \mu\text{mol/L}$
- Impaired liver function
- Significant intestinal disease, e.g., due to radiation or inflammatory bowel disease
- Presence of histologically proved cancer at the prostatic apex (males) or bladder neck (females)
- Presence of metastatic disease
- Lack of patient motivation and/or intellect to follow a strict postoperative voiding regime, to accept possible incontinence (predominantly nocturnal) in the early, and sometimes long-term, postoperative phase
- Lack of compliance to regular routine follow-up
- Physical limitations preventing self-catheterization, e.g., quadriplegia
- Impaired rhabdosphincter or incompetent urethra

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**Table 1: Advantages and disadvantages of orthotopic neobladder and ileal conduit urinary diversions**

Type of urinary diversion	Advantages	Disadvantages
Orthotopic neobladder	No stoma and associated stomal complications Less effect on physical image Comparable or better postoperative sexual function than patients with ileal conduit Potential for normal or near-normal urinary continence	Risk of nocturnal incontinence Need for strict postoperative bladder training regime Technically more difficult surgery Potential complications from urinary waste products reabsorption
Other continent urinary diversion e.g., Indiana pouch	Potential for normal or near-normal urinary continence No nocturnal incontinence No need for a stoma bag The small stoma can be easily covered with a bandage that is, less effect on physical image versus ileal conduit	Complications associated with intermittent catheterization Risk of stomal complications e.g., parastomal hernia Technically more difficult surgery Potential complications from urinary waste products reabsorption
Ileal conduit	Technically simpler surgery Fewer complications No bladder retraining No nocturnal incontinence Well understood by health professionals	Risk of stomal complications, e.g., parastomal hernia and stenosis Urinary incontinence Increased long-term expenses for stoma care

and vesica ileale Padovana (circular). Ileocolonic neobladders include the Mainz pouch and Le Bag pouch, and an example of a sigmoid neobladder is the Reddy pouch.

Formation of a neobladder requires reconstruction of intestinal segments. There are thus two important considerations: (1) The type of the intestinal segment and (2) the construction type. Ileum, colon and sigmoid are commonly used intestinal segments used for neobladder reconstruction. Terminal ileum is more favored among the three as it is more distensible and has larger capacity;<sup>[4]</sup> it therefore stores urine at lower pressures thus there is less risk of causing high-pressure damage to the kidneys. The terminal ileum also experiences more mucosal atrophy in the long term which means reduced risk of metabolic consequences as there will be less electrolyte exchange across the mucosa.<sup>[4]</sup>

The second consideration is the type of construction. Intestinal segments are naturally cylindrical in shape but according to Laplace law [Box 2], this is not the best shape to maintain a low pressure in the reservoir. Due to the smaller radius in a cylindrical reservoir, there will be higher intraluminal pressures at lower volumes. Detubularized bowel may be refashioned to a spherical reservoir; however, the larger radius enables it to contain higher volumes at lower intraluminal pressures.<sup>[5]</sup> The sphere has the smallest surface area for the same volume meaning: (1) This has the smallest risk of metabolic consequences secondary to electrolyte exchange across the gut mucosal lining in the neobladder and (2) a minimal length of intestinal segment is required to form a sphere.

### ELECTROLYTE DISORDERS

The wall of a neobladder is lined with intestinal mucosa which is more permeable to urinary electrolytes than urothelium. Hence, metabolic issues may arise due to extended contact time of urine to the intestinal mucosa compared with incontinent urinary diversion. Urine contains elevated concentrations of potassium, hydrogen and chloride. These ions are absorbed in exchange with sodium and bicarbonate from the blood stream, thus resulting in hyperchloremic, hyperkalemic metabolic acidosis and salt-loss syndrome.<sup>[6,7]</sup> These conditions can manifest clinically with lethargy, fatigue and dehydration. It is important to detect and treat metabolic acidosis early as it can induce calcium resorption from bone and hypophosphatemia thus leading to osteoporosis and osteomalacia. In addition, metabolic acidosis can cause hypercalciuria that increases the

risk of developing renal stones.<sup>[7,8]</sup> Furthermore, urine is more concentrated than intracellular conditions. This promotes fluid shifts from the neobladder walls into the urine and can lead to dehydration.

Other urinary wastes such as creatinine, urea and ammonia excreted in the urine are reabsorbed by the gut mucosa as well. Therefore, impaired renal function is a contraindication to having a neobladder as there will be extra burden on impaired kidneys to excrete reabsorbed these urinary waste products. The same applies to liver function as well because increased burden on an impaired liver to metabolize reabsorbed urinary wastes such as ammonia can increase the risk of liver failure.<sup>[9]</sup>

### NUTRITION

Patients undergoing neobladder formation have a higher risk of experiencing ileus  $\geq 5$  days postoperative than those undergoing ileal conduit formation (14.8% vs. 5.5%,  $P = 0.018$ ).<sup>[10]</sup> Therefore, it is imperative that they have sufficient glycogen stores in their liver by means of pre-operative carbohydrate and protein supplementation, e.g., high-carbohydrate drinks as close as possible to surgery. Adequate dietary fiber postoperatively to reduce constipation and monitoring of vitamin B<sub>12</sub> and folic acid are important due to potential impact on the terminal ileum – the only part of the intestine that can absorb these nutrients – are significantly shorter postoperatively. Terminal ileal reduction also interferes with bile acid reabsorption, resulting in malabsorption of fat which can precipitate diarrhea and dehydration. Such issues are more prominent if the surgery involves resection of the ileocecal valve, as colonic organisms (e.g. bacteroides) can enter the ileum and cleave bile acids from their conjugates; the resultant free bile acids are poor fat emulsifiers.<sup>[7,11]</sup> Patients with a neobladder also need to ensure adequate hydration as they could potentially lose a significant amount of water into the urine.

### CONTINENCE

Neobladders are a form of continent urinary diversion but are not free of continence issues. Continence rates vary with surgical technique, length of time after the operation and time of day. Total continence rates with neobladders range from 22.3% to 63.2% at 12 months postoperatively,<sup>[12,13]</sup> and 17.7–74.5% beyond 40 months postoperatively.<sup>[14,15]</sup> Daytime continence rates vary from 21.4% to 99.0% at 3–48 months postoperatively.<sup>[13-18]</sup> The Abol-Enein and Ghoneim modification of the W pouch, a commonly used technique, recorded a daytime continence rate of 93.3%.<sup>[3]</sup> Interestingly, Sevin *et al.* demonstrated a gradually increasing daytime continence rate with time; at 6, 12, 24, 36 and  $\geq 48$  months postoperatively, daytime continence rates were

#### Box 2: Laplace law for a spherical reservoir

$$P = \frac{2Tw}{R}$$

*P*: Pressure; *T*: Tension; *w*: Wall thickness; *R*: Radius of reservoir

63%, 70%, 76%, 88% and 92%, respectively.<sup>[19]</sup> Furthermore, there were no significant difference in daytime incontinence rates between patients with a modified S-pouch neobladder and a healthy control population without urinary diversion (10% vs. 9.3%,  $P = 0.1$ ).<sup>[20]</sup>

Patients with a neobladder are generally less continent at night than in the daytime. In the nighttime, 18.9–79%, 74%, 23%, 77.6% and 44% of patients were continent at 12, 38 (mean), 44 (median), 48 and 54 (mean) months postoperatively, respectively.<sup>[13-15,17-19,21]</sup> The Abol-Enein and Ghoneim modification of the W pouch has a high nighttime continence rate of 80% at a mean follow-up of 38 months.<sup>[3]</sup> Again, Sevin *et al.* demonstrated a gradually increasing nocturnal continence rate with time; at 6, 12, 24, 36 and  $\geq 48$  months postoperatively, nocturnal continence rates were 55%, 62%, 73%, 85% and 90%, respectively.<sup>[19]</sup> In comparison with healthy subjects of similar age, gender and comorbidities, patients with a modified S-pouch neobladder had a significantly higher rate of nocturnal incontinence (28% vs. 3.7%,  $P = 0.003$ ).<sup>[20]</sup> Nocturnal incontinence is a significant issue as 48% of patients with nocturnal incontinence at least once a week suffered moderate-severe negatively affected sleep compared with 16% of patients with nocturnal incontinence of up to once a month (relative risk 3.0, 95% CI: 2.0–4.7). Furthermore, self-assessed QoL was lower in those patients who had moderate-severe negatively affected sleep than those with minimal adversely affected sleep.<sup>[21]</sup>

Lack of standardization in the definition of continence, different surgical techniques in neobladder reconstruction and variation in patients' record-keeping may account for such a wide range in continence rates between studies. The definition and measurement of continence should be based on an approved scoring system such as the International Consultation on Incontinence Questionnaire–Urinary Incontinence Short Form (ICIQ–UI SF) scoring system. Practicably, patients should keep a diary to record the frequency and severity of daytime and nocturnal incontinence to improve the accuracy of future studies, and this is part of neobladder training in any case.

### NEOBLADDER TRAINING

Laplace law [Box 2] dictates that increasing the radius of a reservoir will increase the wall tension thus inducing more tissue damage. When pressure within a spherical reservoir increases, the wall tension will increase by the same factor if the wall thickness and radius of the reservoir is maintained. In a real neobladder, however, any further distention beyond the full capacity will increase the size and thus the radius of the reservoir, along with stretching the neobladder wall, which

reduces the wall thickness. Over-distension should be avoided, especially in the immediate and early postoperative period to avoid damage to the healing tissues by intensive neobladder training – an important consideration with patient selection.

In the immediate postoperative stage, an indwelling and suprapubic catheter remains in the neobladder postoperatively to allow for adequate surgical recovery before commencing neobladder training. Regular 6–8 hourly flushing of the indwelling catheter with 100 mL of normal saline 0.9% is performed to reduce the risk of catheter blockage. At our institutions, a cystogram is performed at 2–3 weeks postoperatively to confirm that the new reservoir is watertight. Removal of the indwelling catheter and trial of void is then performed under supervision to allow for close monitoring of voided and post-void volumes, blood pH and bicarbonate levels, teaching of neobladder emptying techniques and if necessary, teaching of intermittent self-catheterization techniques. Techniques to void urine from a neobladder are important as it lacks the contractility of a native bladder. We instruct our patients to void in the sitting position, consciously relax the sphincter and pelvic floor muscles and then use a Valsalva maneuver to empty their neobladder. If required, patients may also increase their intra-abdominal pressure by leaning forward or exert gentle manual pressure over the lower abdomen and suprapubic area.<sup>[6]</sup> Pelvic floor muscular awareness and education are also critical in recovery and is well-summarized elsewhere.<sup>[6,9]</sup> As with radical prostatectomy stress incontinence may ensue early, but gradually recovers with correct pelvic floor muscle contraction assisting with strength and control.

The second important consideration is gradual increment of neobladder capacity with a transition from a capacity of 150–200 mL to 400–500 mL in the longer term. During the early stages, frequent neobladder emptying is performed 2–3 hourly daily and 3-hourly timed nightly to avoid overflow incontinence.<sup>[6,22]</sup> Voiding intervals can then be increased gradually over the next few weeks to achieve the aim of voiding every 5–6 h during the day and just once at night. It is also important to note that high post-void residual urine volumes will require the need to void more frequently as the neobladder fills up more rapidly. Patients faced with the issue of inadequate emptying even after performing the correct maneuvers may have to consider intermittent self-catheterization. Patients with higher body mass index are at risk (OR 1.5; 95% CI: 1.06–2.15,  $P = 0.023$ ).<sup>[15]</sup>

### URODYNAMICS

The etiology of incontinence in neobladders has also been investigated by means of urodynamic studies. Multivariate analysis revealed that large post-void residual urine volume, and

frequency and maximum amplitude of uninhibited contractions were the most significant parameters associated with nocturnal incontinence.<sup>[23]</sup> Pharmacotherapy has a role in improving continence. A small trial has yielded promising results with oxybutynin (5 mg 3 times/day) and verapamil (240 mg once daily) with 70% and 55% clinical improvement, respectively.<sup>[24]</sup>

Besides incontinence, some patients experience poor neobladder emptying or “hypercontinence” as well. Certain complications of neobladders such as electrolyte disorders, acidosis, urinary tract infections and pouch calculi formation are more pronounced in such patients. Final bladder shape and length of the bowel segment may affect post-void residual urine volumes. It is important to recognize and teach intermittent catheterization as required.

### SEXUAL FUNCTION

Effects on erectile function and sexual desire are important considerations in cystectomy. Therefore, techniques to preserve the neurovascular bundle supplying the genitalia have been developed to help maintain preoperative sexual function. Bilateral preservation of the neurovascular bundle in ileal neobladder formation has been shown to achieve a 2-year potency rate of up to 60% compared with a rate of 30% achieved with unilateral preservation techniques.<sup>[25]</sup> There are conflicting findings. Protogerou *et al.* found no statistically significant indication of sexual dysfunction in women with nerve-sparing modified S-pouch neobladder and those without.<sup>[20]</sup> Even with nerve-sparing procedures, men with a modified S-pouch neobladder still experienced significantly lower rates of erections (35.5 vs. 83.3%,  $P = 0.003$ ) and decreased erection quality (22.2 vs. 83.3%,  $P = 0.002$ ) than normal subjects.<sup>[20]</sup> A recent case series also supported these findings; Asgari *et al.* found that men experienced significant deterioration in both erectile function and sexual desire postoperatively, irrespective of the type of urinary diversion performed.<sup>[26]</sup>

Between 23.7–35.5% of patients retain adequate erectile function after neobladder reconstruction.<sup>[15,20,26]</sup> Some studies demonstrated that neobladder reconstruction results in better preservation of sexual function when compared with an ileal conduit using the International Index of Erectile Function questionnaire. Specifically, 35.0% of men in the ileal neobladder group were able to achieve and maintain erections sufficient for vaginal penetration throughout sexual intercourse, compared with 9.8% of men in the ileal conduit group ( $P = 0.006$ ). In addition, more men in the ileal neobladder group rated their sexual desire high or very high in comparison with men in the ileal conduit group (45.0% vs. 24.4%,  $P = 0.01$ ).<sup>[26]</sup> Asgari *et al.* also found that more men with an ileal neobladder

reported unaltered sexual desire compared with patients who had an ileal conduit (17.5% vs. 7.2%,  $P = 0.01$ ).<sup>[27]</sup> There are conflicting results from other studies where no difference was found.<sup>[27,28]</sup>

### QUALITY OF LIFE

Quality of life is a very broad term; it is typically subdivided into a number of parameters to help ascertain the effect on an aspect of someone's life. Comparing QoL is affected by the lack of standardization in the use of various questionnaires types among comparison studies and the suitability or relevance of each. Some instruments measure QoL in general whereas some are more specific toward the unique ways urinary diversion can impact on life. The QoL in patients who had neobladder reconstruction are commonly compared to the life experienced by those with an ileal conduit, likely because these are the two most common urinary diversion procedures performed in most locations.

Fujisawa *et al.* compared the health-related QoL using the SF-36 questionnaire in 56 patients and found no statistically significant difference in scoring parameters between patients who had neobladder and those with an ileal conduit. However, patients with either a neobladder or ileal conduit scored significantly lower than the general United States population norm in terms of role-physical functioning and role-emotional functioning.<sup>[29]</sup> In a similar study on 88 Italian men using the SF-36 questionnaire, there was again no statistically significant difference in scoring parameters between patients who had neobladder and those with an ileal conduit. However, patients with either a neobladder or ileal conduit scored significantly lower than the general Italian population norm in terms of role-physical functioning, social functioning and role-emotional functioning.<sup>[30]</sup> Studies using different QoL questionnaires (QLQ) also found similar results. Sogni *et al.* did not find any statistically significant difference in any questionnaire parameters among patients who had a neobladder and those with an ileal conduit when assessed using the European Organization for Research and Treatment of Cancer instruments QoL questionnaire-C30 (QLQ-C30) and QLQ-muscle-invasive BC module (QLQ-BLM).<sup>[31]</sup> In addition to no statistically significant difference in the QoL of patients with a neobladder or ileal conduit, Protogerou *et al.* also found no significant difference when compared to the QoL of a control population (patients without BC) using the QLQ-C30 questionnaire.<sup>[20]</sup>

There are, however, conflicting findings in other studies. In a prospective study by Singh *et al.* using the QLQ-C30 questionnaire, patients who underwent orthotopic neobladder reconstruction reported significantly better physical

functioning ( $P \leq 0.001$ ), role functioning ( $P \leq 0.01$ ), social functioning ( $P = 0.01$ ) and global health status/QoL ( $P \leq 0.002$ ) throughout the first 18 months postoperatively compared with patients who had ileal conduit formation.<sup>[32]</sup> Although the patients who had orthotopic neobladder reconstruction were significantly younger by a mean age of 2-year, there was no significant differences in any of the baseline QoL variables and none of the preoperative QoL domains were correlated with age.<sup>[32]</sup> Using the QLQ-C30 questionnaire, Erber *et al.*, also found significantly better global health status/QoL ( $P = 0.019$ ) and better physical functioning ( $P = 0.018$ ) in patients with an ileal neobladder compared with those with ileal conduit formation.<sup>[10]</sup> Physical and emotional well-being scores in women with a neobladder were also significantly better ( $P < 0.03$ ) than those with a cutaneous ureterostomy when assessed using the Functional Assessment of Cancer Therapy for BC (BL) questionnaire.<sup>[33]</sup> Using a 98-item questionnaire, Asgari *et al.* found a significantly higher global satisfaction rate among those with an ileal neobladder compared with those with an ileal conduit (76.2% vs. 52.8%,  $P = 0.002$ ).<sup>[27]</sup> Contradictory findings were present in a study by Thulin *et al.* who found that 37% of those with an orthotopic neobladder reported that it adversely affected their sleeping patterns, compared with 22% of those with a urostomy. Moderate or much bother due to the daytime and nighttime emptying frequency was statistically significantly higher in those with orthotopic neobladder versus non-continent urostomy, 29% versus 19%, respectively.<sup>[21]</sup> In this study, one possible reason for patients with neobladder not reporting a better QoL than those with ileal conduit is that the higher incidence of sleep disturbances negatively affect the energy level and QoL in the daytime.

## CONCLUSION

Orthotopic neobladder reconstruction has a number of unique advantages and disadvantages as compared with other forms of urinary diversion. This procedure requires comprehensive counseling between the patient and the surgeon to discuss the various considerations of the procedure. The important issues include preventing metabolic complications, managing urinary incontinence especially during the early postoperative stage and ensuring patient compliance to a neobladder training regime. In addition, potential patients should be carefully selected, keeping in mind the contraindications for this surgery in order to reduce the risk of postoperative complications. Continence rates vary widely among studies depending on the time since the operation, type of neobladder reconstruction and definition of urinary incontinence in the studies. Urinary incontinence rates are higher at night than in the daytime, and this reduces sleep quality. In comparison with ileal conduit formation, patients who had orthotopic neobladder

reconstruction surgery reported predominantly comparable or better QoL and sexual function.

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