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Neobladder Voiding Function in Men

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Abstract Following construction of an orthotopic neobladder, the lower urinary tract manifests an altered function. The voiding mechanism in neobladder patients is non-physiologic. To ensure acceptable continence and protect the upper urinary tract, careful patient selection and surgical expertise are required. Although functional qualities of the orthotopic reservoir often remain stable over time, long-term follow-up is necessary as distinct complications are an ever-present concern.

Keywords Orthotopic neobladder · Continence · Nocturnal incontinence · Nerve sparing

Introduction

Incorporation of intestinal segments into the urinary tract was described over a century ago. Orthotopic intestinal bladder replacement was first described in 1951 [1]. However, incontinent reconstruction using an ileal or colon conduit was the gold standard for lower urinary tract reconstruction following cystectomy until the 1980s. The concept of a detubularized, spherical reconstruction, allowing for a low-pressure reservoir, was later described by Kock [2] and led to the advent of the continent cutaneous diversion. Further advances in medical management and surgical techniques have led to the more widespread use of orthotopic neobladders (ONBs) in patients undergoing radical cystectomy (RC) over the last several decades. A better understanding of the intra-operative and perioperative anesthetic needs of these patients, the importance of bowel detubularization and clean intermittent catheterization (CIC), and the expertise gained in preserving the outlet (i.e., preservation of continence) are foremost among factors which make the construction of an ONB a legitimate option to patients undergoing RC [3]. Unlike candidates of bladder augmentation, most candidates for an ONB are continent and neurologically intact and expect to remain so following surgery. Standard RC includes the removal of the distal ureters, urinary bladder, prostate, and the seminal vesicles [4]. This surgery potentially leads to the irreversible transformation of normal urinary storage and elimination. If an ONB candidate *understands* and *accepts* this new reality and no contraindications exist (such as renal failure, hepatic failure, and tumor involving the prostate or bladder neck), then creation of an intestinal bladder substitute may be carried out.

Studies on the long-term functional performance of ONB have generally demonstrated that neobladder functional capacity, continence, and renal function remain stable [5]. Furthermore, the data indicates that construction of the ONB does not compromise oncologic outcome [6]. However, ONB construction is still not globally considered the gold standard for post-cystectomy urinary diversion. The reasons are multifactorial and include lack of evidence from randomized controlled studies demonstrating improved quality of life in patients with ONB versus ileal conduit, patient education, and surgeon preference and experience [7].

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Over the last decade, results of robotic RC using both intra- and extra-corporeal ONB construction techniques have emerged. Such robotic approaches are feasible but appear to be focused at large-volume centers due to the various challenges of the procedure. Debate exists regarding the functional outcomes of the lower urinary tract after intra-corporeal reconstruction with long-term data sparse [8]. However, urodynamic parameters do appear to be similar as evidenced in a recent report evaluating 12 intra-corporeally constructed neobladders with short-term (9.4 months) follow-up [9].

Intestinal Segments

ONBs have been described incorporating both small and large bowels. The inherent physiologic myogenic qualities of intestinal segments are different from those of the detrusor. Intestinal segments involuntarily contract, and both the frequency and the force of the contraction are exacerbated by distension [10]. Furthermore, the contractility profile differs among intestinal segments. Both small and large intestines can demonstrate phasic and tonic contractions. In addition, the colon may also exhibit mass contractions [11].

In contrast, under normal circumstances with an intact bladder, detrusor contraction is voluntary. Initial reservoirs were constructed of tubularized intestinal segments, and although volitional micturition was achieved, intra-pouch pressures and nocturnal incontinence rates were unacceptably high. Introduction of detubularization of the intestinal segments provided advantages for their utilization as bladder substitutes. A more spherical reservoir configuration of these reservoirs meant higher volumes at lower pressures and permitted use of shorter intestinal lengths. In addition, detubularization disrupts the contractile activity of intestinal segments which significantly blunts the circumferential contraction force, therefore improving nocturnal incontinence [12, 13]. The decision of which intestinal segments to utilize as a bladder substitute depends on several factors such as availability, surgeon preference, prior surgery, radiation, patient comorbidities, and age [14]. For patients without significant mitigating factors, ileum has become the segment of choice due to the ease of obtaining the segment and the lower pressures, higher capacity bladders, and less myogenic contractions that are obtained with ileal ONBs [15, 16].

The Altered Lower Urinary Tract Physiology in Patients With ONB

The male lower urinary tract (LUT) consists of the bladder, bladder neck, prostate (prostatic urethra), membranous urethra, and penile urethra. Innervation of the LUT is via three groups of neural networks: the parasympathetic system, sympathetic system, and somatic nerves. The sacral spinal cord (S2–S4) is the origin of the parasympathetic autonomic system via the pelvic nerve and the somatic via the pudendal nerve. The origin of the sympathetic autonomic nervous system is in the thoracolumbar (T10–L2) spinal cord via the hypogastric nerve. The urinary bladder is innervated by the autonomic system. Efferent innervation of the bladder wall is primarily parasympathetic with the trigone and bladder neck supplied by the sympathetic system. Afferents from the bladder travel by both parasympathetic system and sympathetic system via the pelvic plexus [17]. No consensus exists regarding afferent and efferent innervation of the external urethral sphincter [18]. While some authorities believe that the external sphincter is innervated solely by the somatic system via the pudendal nerve, others have suggested a joined somatic autonomic innervation. Alternate theories have been postulated in which the external urethral sphincter is exclusively innervated by nerves originating from the pelvic plexus [19, 20]. Some data demonstrates that the striated urethral sphincter has a dual somatic innervation by both the pudendal nerve (extra-pelvic) and an extra-pudental and intra-pelvic branch [21]. Additional studies of the external urethral sphincter neuroanatomy suggest that sensation of the membranous urethra is via branches of the dorsal nerve of the penis close to the prostatic apex and is prone to damage either as a result of hemostatic sutures to the dorsal vein or anastomotic sutures. Interestingly, these nerves are not symmetrical [19].

If the innervation of the distal sphincteric element does have an intra-pelvic component, then applying the nerve-sparing technique to patients undergoing cystoprostatectomy may have a beneficial role in achieving and maintaining continence. Potential mechanisms whereby a nerve-sparing technique may improve continence include the following: preventing damage to the sensory input from the membranous urethra by preventing autonomic denervation leading to smooth muscle dysfunction [22, 23].

The distal, external sphincter is composed of a combination of smooth muscle and striated muscle (rhabdosphincter). At the level of the membranous urethra, the rhabdosphincter is most pronounced and displays an “omega” shape with the open portion posteriorly situated. The smooth muscle component circumferentially encompasses the urethra from the bladder neck to the proximal bulbar urethra. Up to 40 % of the total urethral functional length is covered by apical parenchymal prostatic tissue [23]. Therefore, at the time of cystectomy and/or prostatectomy, preparation of the distal sphincteric element requires meticulous dissection. Although controversy exists as to which component of the external sphincter is most important in conferring continence (smooth muscle versus rhabdosphincter) post-cystectomy, there is consensus regarding the importance of an adequate functional urethral length [23, 24•].

Under normal physiologic conditions, continence is maintained by vesicourethral reflexes modulated by higher centers in the brainstem and brain in the setting of intact end organ tissues (urinary bladder and outlet) [25]. The process of maintaining continence throughout bladder filling is labeled the guarding reflex, which is composed of two components. The involuntary component increases sphincter tone at low bladder volumes without sensory awareness along with a voluntary component that further increases sphincter tone once bladder sensory threshold is reached [26•]. Following cystoprostatectomy, the afferent arm of these reflexes is abolished. In patients following ONB construction, continence is dependent on an anatomically and neurologically intact distal sphincter and potentially on an intact urethral sphincter reflex. In this reflex, the afferent arm may be reliant on intact membranous urethral sensation [27, 28].

Living With an Orthotopic Intestinal Neobladder

Preservation of voiding function has a profound effect on the quality of life in patients with an ONB. For successful voiding with an ONB, conditions should replicate the normal physiologic state as feasible. In the storage phase, bladder capacity should be approximately 450–500 ml at pressures of approximately 15 cm/H_2o or less. This is achieved by adequate intestinal segment length and detubularization. For an efficient voiding phase, the ONB should be directly anastomosed to the urethra and positioned in the most dependent portion of the pelvis [5]. Voiding frequency should be less than nine times a day with continence hopefully maintained in between voids. Following ONB construction, patients often need to learn alternate methods of voiding involving pelvic floor relaxation combined with increasing intra-abdominal pressure [29].

Continence status of an ONB candidate is dependent on several factors such as surgical technique, patient age, intestinal segment utilized, and the patient's adherence to timed voiding. Following reconstruction, it may take up to a year for the ONB to reach functional capacity. During that time interval, diurnal continence may continue to improve [30]. Patients are often instructed regarding timed voiding with increasing intervals between voids until functional capacity is reached. Initially, pelvic floor relaxation may be optimally achieved by voiding in the sitting position. Use of pelvic floor physical therapy may provide a helpful adjunct, instructing patients on pelvic floor strength to improve continence as well as methods to promote pelvic floor relaxation to accommodate neobladder voiding.

Multiple studies have reported on diurnal continence rates of males following ONB construction (Table 1). Daytime and nighttime continence rates ranged from 68 to 97 and 30 to 96 %, respectively [31]. Follow-up was exceptionally variable from 2 to 8 years. Experience with Studer-type ONB confirmed that functional reservoir capacity remains stable for at least 9 years following surgery, and there is no evidence suggesting loss of function with longer follow-up [5].

Age at the time of cystectomy and reconstruction appears to directly correlate to continence. One study reports on a dramatic decrease in striated muscle cells in the rhabdosphincter of older patients. This muscle decrease is postulated to be due to apoptosis [32]. Decreasing muscle mass reflects clinical outcomes with lower ONB continence rates noted in patients greater than 65 years of age. In addition, continence rates were improved in patients who underwent nerve-sparing cystectomy [33]. However, continence rate between studies varies depending on how and when it is measured. A recent prospective study comparing four types of intestinal reservoirs (three ileal and one colonic) showed a lower rate of diurnal continence than previously accepted. Daytime and nighttime continence rates for ileal ONB, calculated by 24-h pad weight and voiding charts, were 68 and 30 %, respectively. Continence rates in colonic ONB were even lower [16]. Few studies provide information regarding the acquisition of continence evaluation, underscoring the shortcomings and challenges of reporting and comparing continence rates of patients following ONB construction. Validated quality of life (QOL) questionnaires are available for evaluating continence and bother following the construction of ONB [34]. However, the lack of standardization of QOL questionnaires, the variation in patient record keeping and reporting, and the lack of an accepted definition of continence make comparison between different studied cumbersome.

To accurately measure the impact of continence influencing surgery such as ONB, several endpoints may be required. An objective measure of leakage may be assessed by pad size and number used, whether pads are used during the day, night, or diurnally. However, pad number and weight do not always reflect the degree of bother that is associated with the incontinence. One may conclude that the impact of incontinence on a person is not merely an objective measure of urine leakage but additionally has a psychosocial component potentially influenced by age, etiology, and other medical and social factors.

Urinary elimination after the construction of an intestinal neobladder is completely transformed. Normal sensation of reservoir fullness is absent, as afferents from intestinal segments do not synapse with neurons typically associated with bladder awareness in the central nervous system. These patients usually sense reservoir fullness as a vague sensation of suprapubic discomfort. The desire to void may be felt at the base of the penis as small amounts of urine reach the membranous urethra or beyond [35]. Although the ability to voluntarily relax the pelvic floor is preserved, reservoir contraction has a minor role in urine elimination. Voiding in most patients with intestinal substitutes is primarily by Valsalva effort. One study evaluating neobladder patients identified

Table 1 Functional studies of male patients with an orthotopic neobladder

Reference	Technique	Number of patients	Continence (%)		Mode of continence assessment	Median follow-up	Average neobladder capacity (ml)	Time of assessment (years)
			Day	Night				
Barre P. [46]	Camey II	109	92.6	74.3	NR	32	530	NR
Cancrini A. [47]	Studer	89	97	74	NR	28	330	1
Elmajian D. [48]	Kock	295	87	86	NR	42	NR	1
Hautmann R. E. [49]	Hautmann	290	83.7	66.3	Standardized questionnaire	57	460	1
Steven K. [50]	Kock	166	81[a]	75[a]	Interview Protective devices Provocation test	32	411	1, 3 ,5
Parekh D. J. [51]	84 ileal ONB, 16 colonic ONB	100	93	71	Patient interview and charts	24	NR	NR
Madersbacher S. [52]	Studer	83	90	96	NR	95	473	5
Sevin G. [53]	Hautmann modified	116	92	90	NR	76.8	550	4
Paananen I. [16]	66 ileal 12 colonic	78	68 0	30 0	24-h pad test, UDS, US, interviews	NR	500 684	1

[a] Time of assessment at 1 year

two voiding patterns of either Valsalva throughout voiding and a second pattern where Valsalva at the end of micturition [36].

An important issue to follow after ONB construction is incomplete emptying of the reservoir. The incidence of neobladder emptying failure has been reported to be as high as 11.5 %; however, that was defined as a post-void residual (PVR) above 100 ml [37•]. In fact, most patients with incomplete emptying of the neobladder are asymptomatic or can be managed with CIC several times a day as needed. However, incomplete emptying may be a sign of additional pathology including the following: tumor relapse, anastomotic stricture, urethral stricture, cystolithiasis, reservoir outlet kinking, or dysfunctional voiding [5, 37•]. Meticulous evaluation is indicated if a patient evolves from a state of adequate emptying to new onset state of incomplete emptying. In addition to standard history and physical examination, assessment of incomplete emptying may include urethral washing/cytology, urodynamics, cystoscopy, cystogram, and ultrasound. Most patients with urinary retention due to local tumor recurrence suffer from pelvic pain [31]. However, a local recurrence along the urethra, though rare, could certainly lead to issues with emptying. Recurrence is often identified prior to overt anatomic obstruction with a urethral washing/cytology [5]. Recurrent episodes of gross hematuria, with or without fever, may be suggestive of cystolithiasis, urethral recurrence, urethral trauma (for those patients that perform CIC), and urethral or anastomotic stricture.

In cases of de novo incontinence, one should rule out dysfunctional voiding. Initial evaluation begins with a PVR. Dysfunctional voiding has an incidence of approximately 3.5 % and is most commonly associated with gradual onset. These patients are usually not mechanically obstructed but fail to relax the pelvic floor during voiding [37•]. Such patients will usually describe an easier ability to void while defecating. The etiology of dysfunctional voiding in this patient population is poorly understood, and all patients will eventually need to empty their reservoir by CIC if pelvic floor physical therapy is unable to improve the situation [31].

The ability to adequately void with a neobladder appears to be related to several factors. A prior study compared voiding parameters in two groups defined as “fine voiders” and “poor voiders.” Fine voiders and poor voiders were defined by a flow rate of above or below 15 ml/s, respectively. This study showed that fine and poor voiders strained an average of 1.5 and 6.3 times to expulse 100 ml of urine, respectively. The average maximal flow rate of fine and poor voiders was 26.2 and 9.4 ml/s, respectively. In addition, cystography of fine voiders displayed funneling of the outlet in both filling and rest while poor voiders showed neither. The authors concluded that the urethra should be anastomosed to the most caudal part of the neobladder to achieve optimal voiding in ONB patients [38]. Tubularizing the neobladder neck (source of outlet resistance) is another potential cause of emptying failure. This modification may lead to improved continence rates with the trade-off of a greater risk of urinary retention [39]. Furthermore, recent data comparing three types of nerve-sparing techniques in patients undergoing RC and construction of an ONB noted a significantly higher incidence of CIC in the capsule-sparing RC compared to seminal-vesicle-sparing RC and nerve-sparing cystovesicle prostatectomy [40]. Taken together, it seems that in order to prevent functional obstruction, in patients following ONB construction, a minimization of any potential outflow resistance should be obtained between the most dependent part of the neobladder and the urethra.

Nocturnal Incontinence

The incidence of nocturnal incontinence is 15 to 40 % depending on how the incontinence is measured and characterized [41]. Unlike the normal physiologic state, the reservoir and outlet in patients after the construction of an ONB are not a functional unit. Therefore, the functional qualities of each component as well as patient behavior may impact nocturnal continence. Although detubularization has decreased the incidence of nocturnal incontinence by reducing bladder storage pressures, such leakage remains a bothersome issue. There appears to be several factors that contribute to this problem.

An increase in nocturnal urine production can occur, following ONB construction, due to an osmotic pseudo-diuresis secondary to acidic, concentrated urine. A decrease in patient compliance with timed voiding that may lead to overflow incontinence. There is also evidence suggesting an increase in bowel activity during sleep [42]. Finally, following the creation of an ONB, patients cannot increase their sphincter tone as vesicourethral reflexes are abolished. Since the urethra-sphincter reflex is a conscious reflex, nocturnal incontinence may occur once intra-pouch pressures overwhelm the static urethral closing pressure at night when the patient's level of consciousness is decreased [43]. It appears that maximum urethral closing pressure (MUCP) is the primary component responsible for daytime continence in patients with an ONB. However, Koraitim et al. suggest that nocturnal incontinence depends on three reservoir parameters: maximal contraction amplitude, baseline reservoir pressure at mid capacity, and MUCP [11]. It is important to evaluate patients with nocturnal incontinence who are bothered enough to consider therapy. A study of these patients suggested that approximately one third actually display failure to empty as a result of mechanical or dysfunctional voiding. Increasing the outlet resistance of these patients not only may improve their incontinence but also may result in the need for CIC or possibly place them at risk of upper tract deterioration if the ONB demonstrates elevated storage pressures [44]. For those patients that primarily leak at night due to inadequate nocturnal sphincteric function, placement of an artificial urinary sphincter is a viable option. In addition, if the sphincter is not needed for daytime continence, it can be deactivated during the day [45].

Conclusion

The voiding behavior and continence of patients with an ONB depend independently on the functional characteristics of both the reservoir and the outlet. Bladder emptying is primarily accomplished by a combination of Valsalva effort and outlet relaxation. A constructed neobladder is unable to form an adequate, sustained contraction as is typical with an intact bladder. Patients with a deterioration of their voiding behavior after ONB merit further anatomic and functional investigation.

Compliance with Ethics Guideline

Conflict of Interest Dr. Ginsberg reports grants and personal fees from Allergan and grants from Medtronic, outside the submitted work; Dr. Rosenberg has nothing to disclose.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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