Curr Urol Rep (2017) 18: 5
DOI 10.1007/s11934-017-0652-4

Treatment of Pelvic Floor Disorders Following Neobladder

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Published online: 30 January 2017

Abstract Radical cystectomy remains the gold standard treatment for organ-confined high-grade recurrent or muscle-invasive bladder cancer. Orthotopic neobladder urinary diversion following cystectomy represents an option for patients wishing for continent urinary diversion. Female patients who undergo radical cystectomy with orthotopic bladder substitution are at risk for developing both common and neobladder-specific disorders of the pelvic floor, including urinary incontinence, hypercontinence, vaginal prolapse, and neobladder-vaginal fistula. Each of these sequelae can have significant impact on the patient's quality of life. Due to the increased frequency of orthotopic neobladder creation in women, subspecialty urologists are more likely to confront such pelvic floor disorders in bladder cancer survivors. This review presents the most current information on the treatment of pelvic floor disorders after orthotopic bladder substitution.

Keywords Neobladder · Fistula · Prolapse · Cystectomy · Incontinence · Urinary retention

Introduction

It is estimated that 25% of all new bladder cancer diagnoses in 2016 will occur in women [1], who are additionally more likely to present with advanced disease requiring invasive therapy [2]. Radical cystectomy with urinary diversion remains the gold standard of treatment for recurrent high-grade or muscle-invasive bladder cancer. Options for urinary diversion primarily include conduits, continent cutaneous diversion, and orthotopic neobladder (ONB). The proposed benefits of ONB are replication of "normal" voiding, possible improvement in body image and quality of life, and elimination for the need for external ostomy. ONB was initially performed only in males due to concern for continence in females. However, further description of female sphincter anatomy suggested ONB would be a reasonable option for diversion in women as well [3, 4]. As such, up to 70% of women undergoing cystectomy are candidates for ONB diversion [5].

Pelvic floor disorders and ONB-specific complications in the female patient include urinary incontinence, urinary retention (i.e., "hypercontinence"), vaginal prolapse, and neobladder-vaginal fistula (NVF). Multiple studies demonstrate large variations in the incidence of these ONB complications [6, 7]. Nonetheless, each of these entities can have a profound impact on quality of life. This review presents the most current information on the treatment of pelvic floor disorders after ONB substitution.

Operative Considerations

Naturally, many authors have focused on operative techniques to improve functional results after ONB. The preservation of pelvic organs may confer functional benefit without compromising oncologic efficacy [8–11]. Data suggests that the urodynamic profiles are comparable between women with and without uterine preservation [10]. Furthermore, Gross et al. recently reported their experience in urethral pressure profiles performed before and after surgery in order to

This article is part of the Topical Collection on *Female Urology*

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evaluate what factors influence voiding dysfunction postoperatively. The authors demonstrated that patients with uterine preservation postoperatively had a longer functional urethral length, higher urethral closing pressure, and improved continence [11]. Other studies indicate prior or concomitant hysterectomy was the only predictor of postoperative daytime urinary incontinence, while additional data demonstrated age >65 was associated with incontinence after surgery [9, 12].

In addition, there are reports of uterine preservation permitting preservation of fertility, with delivery by planned cesarean section [7]. Preservation of the anterior vaginal wall at the time of cystectomy has also been shown to improve sexual function [7, 10]. In contrast, injury of the anterior vaginal wall at the time of cystectomy may be one of the primary risk factors for NVF formation [13].

Combined with preservation of the uterus and vagina, several authors have proposed a nerve-sparing technique to improve continence [11, 14, 15]. Cadaveric studies have suggested that the autonomic nervous supply to the proximal urethra via the pelvic nerve and somatic nervous supply to the rhabdosphincter via the distal pudendal nerve are at risk during extensive dissection of the posterolateral vaginal wall and anterolateral rectum [16]. Limitation of vaginal dissection at the 4 and 8 o'clock positions, when oncologically feasible, may limit damage to these nerves and preserve urethral function [15, 17]. Return of continence by initially incontinent women following cystectomy and ONB is postulated to be related to resolution of neuropraxia in the absence of direct surgical injury [11]. This phenomenon may be limited by avoiding significant tenting of the rectum during dissection [16]. Furthermore, limited dissection distal to the bladder neck to limit direct injury to rhabdosphincter is of utmost importance in preserving continence. Nerve preservation is unlikely to offer significant benefit if direct damage to the rhabdosphincter occurs [7, 11].

Incontinence

The prevalence of daytime urinary incontinence after ONB has been reported, in the majority of cases, to be from 10–27% [6–12, 14]. However, a retrospective review of 49 women following cystectomy with ONB identified the long-term prevalence of daytime urinary incontinence (stress urinary incontinence) to be 43% [9]. These authors surmise that the higher rates in their study relative to previous reports suggest that the true incidence of incontinence had generally been underreported. The main cause for the variability across studies is likely due to a lack of standardization in reporting outcome data.

Preoperative evaluation can aid in reducing the risk of stress urinary incontinence (SUI) after ONB. One study found the severity of daytime incontinence was only associated with preoperative SUI [9]. Preoperative urethral pressure profiles have been shown to correlate with postoperative urethral pressure profiles and continence, highlighting that preoperative continence status predicts postoperative functional outcomes. Likewise, women who have previously received a mid-urethral sling for SUI should be considered high-risk for incontinence after ONB. Therefore, preoperative incontinence, with or without previous interventions, should be considered a relative contraindication to ONB.

Nocturnal incontinence is more common with a reported prevalence of 16–67% [6–12, 14]. This form of incontinence appears to have a marked impact on quality of life. One study in which a cohort of 74 women completed a health-related quality of life questionnaire concluded that nighttime incontinence had a greater impact on quality of life than urinary retention [18]. Furthermore, nocturnal incontinence had the greatest impact social functioning domain section of the quality of life assessment. The impact of daytime incontinence on quality was not assessed independently.

Most studies have focused on reporting the prevalence of incontinence after ONB rather than quantifying it [6]. However, one study categorized patients with daytime incontinence into mild (≤1 pad/day), moderate (2–4 pads/day), and severe (≥5 pads/day, required intervention, or deemed severe by surgeon) [9]. These authors found that 62% of their cohort had severe daytime incontinence. Although objective severity grading was not as clearly defined for nocturnal incontinence, the prevalences of mild, moderate, and severe nocturnal incontinence were reported to be 59, 7, and 15%, respectively. The study had 19% of their population in which nocturnal incontinence was not assessed.

Treatment of incontinence in women after ONB can be very challenging for the urologist. Prior to initiating treatment, it is important to rule out neobladder-vaginal fistula (NVF) or concurrent hypercontinence with overflow incontinence. In the absence of concomitant conditions, therapy follows an algorithm similar to that for stress urinary incontinence in a woman without cystectomy. First-line therapy of mild incontinence involves pelvic floor rehabilitation and lifestyle modification. However, this often results in only limited improvement [14], and many women will be bothered enough to pursue other treatment options.

Urethral bulking agents comprise a minimally invasive, office-based surgical option [13, 14, 19]. Unfortunately, results have been modest, with complete resolution of incontinence after bulking agent reported in only 0–16% [13, 14, 19]. In one study, 67% of women experienced a modest but transient improvement in incontinence, suggesting the need for repeated injections [14]. However, Wilson et al. reported 50% of women experienced no improvement after 2 injections [19]. Although the clinical benefits may be limited, avoidance of needle passage in the retropubic space as is generally required for retropubic slings is a certain benefit [13].

Nonetheless, bulking agents may best be reserved for women with mild SUI who do not wish to undergo or are not candidates for more invasive therapies.

Studies of midurethral synthetic and pubovaginal slings (PVS) have also generally reported disappointing and even disastrous results [13, 14, 20]. Quek et al. reported on four patients undergoing PVS after radical cystectomy. Two suffered major complications, including one who developed an entero-neobladder fistula and another who developed an enterocutaneous fistula with resultant sepsis and death. The authors concluded that dissection in the retropubic space should be avoided, and that infrapubic bone anchors represent a more desirable option [20]. A more recent study reported success with PVS placed subperiosteally to avoid injury to the neobladder [14]. When performed in the context of a NVF, an additional benefit of PVS is an additional layer to bolster fistula repair. A common consequence of PVS, particularly in women with ONB who universally void by Valsalva effort, is urinary retention, and patients should be counseled regarding this risk and the possible need for intermittent catheterization [20].

Use of transobturator slings (TOS) has also been reported; however, as with PVS in this population, data is primarily limited to case reports and small case series. Carmel et al. performed TOS in one patient who experienced great improvement, but not resolution, in her SUI [13]. Another group performed synthetic or autologous TOS in four patients. One of these four patients experienced significant improvement, however did remain incontinent [14]. Although not reported in either of these case reports, use of synthetic slings in this population may be associated with an elevated risk of erosion. Furthermore, vaginal atrophy and short urethral length resulting in intrinsic sphincteric deficiency (ISD) may increase the risk of vaginal mesh extrusion and sling failure, respectively, with synthetic transobturator slings [13]. Incontinence that is refractory to less invasive treatment options may be managed by conversion to incontinent diversion or continent catheterizable diversion such as the Indiana pouch.

In contrast to daytime incontinence, which is primarily SUI secondary to ISD, nocturnal incontinence is thought to occur due to pouch overdistention, physiologic diuresis, and relaxation of the rhabdosphincter during sleep. One study found only age to be associated with the presence and severity of nighttime incontinence, which is frequently present even in the absence of significant daytime incontinence [10]. Straight catheterization prior to bedtime and potentially one to two times overnight is the mainstay of treatment.

Hypercontinence

Urinary retention after ONB, or hypercontinence, is much more common women, occurring up to 69% of patients, and is a frequently cited reason for avoidance of ONB in women altogether [21]. Hypercontinence can lead to overflow incontinence, increased voiding pressures, potential upper tract damage, bladder stone formation, neobladder overdistention, or neobladder damage. Hypothesized causes of hypercontinence are dyssynergia, overly capacious reservoir, anastomotic stricture, or urethral "kinking," possibly related to anterior vaginal prolapse, or "neocystocele." Although it has been traditionally thought that neocystocele altered the normal anatomy and led to retention [11], the occurrence of anterior prolapse primarily in patients straining to void suggests neocystocele may be the result of obstruction rather than its cause [11, 21].

When Gross et al. performed urethral pressure profiles on women before and after cystectomy with ONB, the authors found that patients with incontinence and elevated post-void residual (PVR) were more likely to have shorter functional urethral lengths and lower maximal urethral pressures than patients who were continent with elevated PVR [11]. The authors suggested these patients either have a hypotonic proximal urethra acting as a flap valve or a failure of urethral relaxation during attempted voiding. In contrast, women who were continent and had elevated PVR had longer functional urethral length and higher maximal urethral pressures. Women in this population were frequently able to void to completion postoperatively but gradually developed increased PVR. On urethroscopy, these patients were deemed to have a tight proximal urethra which in some patients was successfully managed with transurethral resection of the most proximal aspect of the bladder neck and urethra [11].

In general, cystourethroscopy should be performed to rule out anastomotic stricture in women with hypercontinence. In the absence of bladder neck contracture necessitating treatment, clean intermittent catheterization remains the primary option for women with elevated PVR after ONB. In the setting of hypercontinence, women can have varying degrees of associated incontinence while others may be totally reliant on catheterization to void [11, 21], and frequency of catheterization may be adjusted on an individual basis to permit regular emptying and prevent overdistention and overflow incontinence.

Prolapse

Scant literature exists regarding pelvic organ prolapse (POP) after ONB. The incidence is likely underreported, but one series of 78 predominately younger (mean age 42) women undergoing radical cystectomy/ONB in Egypt for squamous cell carcinoma secondary to schistosomiasis reported an incidence of vaginal stump prolapse of 6% [7]. As previously discussed, vaginal prolapse of the neobladder, i.e., "neocystocele," may be either a consequence or a cause for

voiding dysfunction. Obstructive voiding from proximal urethral hypotonicity or obstructing mucosal folds can lead to increased Valsalva pressure that results in weakening of the pelvic floor [11, 21]. Additionally, once the prolapse has occurred, the resultant obstruction may worsen voiding dysfunction. Dynamic MRI studies demonstrate that during micturition, the neobladder may descend to approximately 2 cm below the pubic symphysis, changing the urethral-neobladder angle by 18° and potentially impairing emptying [21]. Therefore, POP after ONB has clinical relevance beyond the bother associated with a vaginal bulge.

Several authors have proposed mechanisms to help prevent POP in this population. Uterine- and vaginal-sparing surgery may prevent POP by preserving pelvic support mechanisms and hormonal support in premenopausal women in whom the ovaries are spared. Because patients with preoperative POP are especially susceptible to developing hypercontinence following surgery [7], prophylactic POP repair at the time of cystectomy may be of benefit [22–24]. An omental or peritoneal flap between the neobladder and vagina has been proposed as a mechanism to both prevent fistula formation and to act as a posterior support mechanism to help prevent migration of the neobladder. Others have suggested prophylactic abdominal sacrocolpopexy or sacrospinous fixation at the time of cystectomy [22, 23].

One study randomized women to either receive sacrocolpopexy with polypropylene tape or no POP procedure [22]. The authors reported improved functional outcomes with sacrocolpopexy. Another case report of prophylactic sacrospinous mesh fixation during laparoscopic cystectomy and ONB reported no prolapse or mesh complications at 30 months postoperatively [23]. It is important to note that despite these two small series not reporting any mesh-related complications, the use of synthetic mesh may be especially risky in this patient population. In the context of risk factors such as intestinal spillage inherent to ileal neobladder creation and multiple healing neobladder suture lines, autologous fascia may be a safer, though likely less durable, option. Furthermore, prophylactic placement of mesh seems perilous in the absence of better evidence, and therefore avoidance of ONB diversion in patients with pre-existing POP may be prudent given the likelihood of hypercontinence and limited options for safe, durable repair.

As in vaginal prolapse in the absence of prior cystectomy, new onset POP after ONB is treated based on symptoms, with conservative therapies preferable as initial management. A woman without evidence of obstructive voiding who is not bothered by the prolapse can simply be followed to ensure retention does not become a problem in the future. Those women who require treatment of POP who fail pessary management may be able to be repaired transvaginally. Due to the shortened vaginal vault, pessaries often have limited efficacy in the ONB population. Options include sacrospinous or ileococcygeus fixation or colpocleisis. However, POP repair may not result in resolution of voiding dysfunction in half of women and may have an even greater likelihood of recurrence than typical native tissue repairs, and patients should be counseled accordingly [21]. Transabdominal sacrocolpopexy with autologous fascia may represent another option that obviates concern for mesh erosion [25].

Neobladder-Vaginal Fistula

Neobladder-vaginal fistula is one of the most feared complications from radical cystectomy with neobladder creation, as it is associated with potentially devastating social and emotional detriment. NVF after cystectomy/ONB has a reported incidence of 3–10% [8, 10, 13, 14, 26–29]. NVF can occur very early or many months after cystectomy [13, 14, 26] and has been reported to occur spontaneously or after urethral injection of bulking agents [14, 26].

NVF may be incorrectly diagnosed as SUI [26]. Furthermore, SUI and NVF often occur simultaneously, and care needs to be taken to obtain an accurate diagnosis. In a recent study, Bailey et al. found that 50% of their patients with incontinence were found to have a NVF. Of the patients with NVF, only 71% had continuous incontinence, suggesting the absence of continuous incontinence does not rule out the presence of NVF [14].

Risk factors for NVF formation are injury to the anterior vagina at time of cystectomy, lack of well-vascularized tissue between the neobladder and vagina, overlapping suture lines, poor tissue vascularity after radiotherapy, and local recurrence [9, 13, 26]. However, damage to the anterior vaginal wall appears to be the most important factor. Many authors have proposed several surgical techniques to limit this risk factor, including sparing the anterior vaginal wall, placing an omental or peritoneal flap between the bladder and vagina at the time of cystectomy, avoiding overlapping suture lines, and a double-layered vaginal cuff closure [6, 9, 13, 26, 28].

There are multiple ways to diagnose a NVF. Physical examination may demonstrate leakage of urine from the vagina without leakage of urine from meatus. A cystogram and/or dye test can be a useful adjunct to the physical exam and may highlight multiple fistulous tracts, whereas a cystogram with an open bladder neck is more indicative of SUI. A dye test alone cannot accurately discern the location of the fistula but may confirm its presence. Vaginoscopy may also permit visualization of the tract. Cystoscopy can be also helpful but represents a less sensitive modality in diagnosis of NVF. Voiding radiography and CT urography have also been utilized when the diagnosis of NVF is suspected but elusive [13, 14, 28].

The approach to fistula after neobladder involves many of the same concepts as native vesico-vaginal fistulas:

circumferential dissection of the fistulous tract, multiple layer closure, tension-free closure, non-overlapping suture lines, and the use of tissue interposition when possible. Because the wall of the neobladder is much thinner than a native bladder, and the patient's vagina is often atrophic and immobile, vaginal repair may be especially challenging but nevertheless remains an option.

Ali-El-Dien et al. suggested an abdominal approach is preferred in women with vaginal atrophy or large fistulas because this approach permits omental interposition [28]. In contrast, Carmel et al. reported excellent outcomes with a transvaginal approach despite larger fistula size and/or vaginal atrophy [13]. The authors instructed patients to use vaginal estrogen cream preoperatively to improve tissue quality. Furthermore, they reported being able to achieve adequate dissection and mobilization of the vaginal wall and tissue interposition with vaginal wall, omental flap, or Martius flap [13]. The authors reported success with transvaginal repair for fistulas located at both the urethral-neobladder anastomosis (UNA), which is the most common site of NVF [13, 14, 29], and the distal anterior vaginal wall. However, another series reported success in only 4/9 (44%) of women with transvaginal repair of NVF at the UNA, whereas all 4 women with fistulas at the anterior vaginal wall experienced successful repair [29]. Successful transvaginal repairs have also been described with native multiple-layer closure without tissue interposition [26, 27] and use of autologous pubovaginal sling at the time of the operation for an additional layer of closure and potentially treat coexistent SUI [14]. Regardless of approach, it is important not to injure the rhabdosphincter during dissection to avoid new onset incontinence; however, in general, the risk of postoperative incontinence via a number of mechanisms is great enough that it is prudent to counsel patients about the possibility of incontinence after NVF repair and the need for subsequent re-operation [13].

Conclusion

Radical cystectomy with orthotopic neobladder is an option for urinary diversion in women requiring cystectomy but is associated with a variety of pelvic floor disorders not generally present with other forms of diversion. Women undergoing ONB are predisposed to daytime incontinence, nighttime incontinence, hypercontinence, pelvic organ prolapse, and neobladder-vaginal fistula. In general, experience in managing these complications is exceptionally limited and often discouraging. Subspecialists tasked with addressing these complications may be encouraged to engage their colleagues to assist with management decisions and report results. In general, conservative therapies are preferred before moving to more invasive surgical treatments, which confer greater risk but may have similarly disappointing results. In especially challenging and devastating complications, conversion to incontinent diversion remains an option that may alleviate symptoms and markedly improve quality of life.

Compliance with Ethical Standards

Conflict of Interest Nathan Littlejohn, Joshua A. Cohn, Casey G. Kowalik, and W. Stuart Reynolds each declare no potential conflicts of interest.

Melissa R. Kaufman is a course director for Boston Scientific and investigator for Cook-Myosite.

Roger R. Dmochowski is a consultant for Medtronic, Allergan, and Axonics.

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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