



Voiding and Continence Problems after Radical Cystectomy and Orthotopic Neobladder in Women: A Mini-Review

Mohamed H Zahran and Bedeir Ali-El-Dein*

Department of Urology, Urology and Nephrology Center, Egypt

Abstract

Orthotopic neobladder has become the standard of care after radical cystectomy in select women with muscle invasive bladder cancer. Proper understanding of the natural history of bladder cancer and functional anatomy of female urethra were the cause of its application in women. Continence and voiding problems are still the most bothering symptoms that affect a significant proportion of women. It adversely affects patients' health related quality of life. Proper patients' evaluation and identification of possible risk factors is mandatory before decision making in order to reduce the possible risk of continence trouble.

Introduction

More than 20 years ago, many centers started to provide bladder cancer female patients with Urethral-Sparing Radical Cystectomy (USRC) with orthotopic urinary diversion (ONB) [1]. This did not gain the rapid clinical acceptance as in men because of the previous believes that urethrectomy is an integral part of cystectomy in female for many reasons. The argument was the possible risk of urothelial tumour recurrence in the remaining urethra, the higher risk of complications including fistula formation with the vagina and the possible high risk of incontinence and voiding problems. With proper understanding of the anatomy of female urethra and continence mechanisms together with vast researches that confirmed the oncological safety of urethral-sparing as long as absence of bladder neck involvement by the tumour, this encouraged urologist to provide their patients with urethral-sparing cystectomy and orthotopic neobladder (ONB) [2]. Currently, ONB has become the standard of care after USRC in select women with bladder cancer [3]. It has been estimated that 80% of men and 65% of women undergoing RC for bladder cancer are eligible for ONB [4]. Here we try to emphasize on the functional outcome of ONB in women especially continence status after it has been a common practice.

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*Correspondence:

Bedeir Ali-El-Dein, Department of urology, Urology and Nephrology Center, Mansoura, Egypt,
E-mail: balieldein@yahoo.com

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Evolution of urinary diversion in women

Since the first reported urinary diversion (UD) using segment of the bowel by Simon in 1852, innovative surgeons have investigated for the best form of UD [5]. The evolution of urinary diversion has developed along 3 paths: non continent cutaneous diversion (ileal loop and colonic loop), continent cutaneous diversion and orthotopic urinary diversion to the native urethra [6]. Ureterosegmoidostomy is the oldest form of urinary diversion and it remained the diversion of choice till the late 1950s, when Bricker refined and popularized the ileal loop conduit. It has become the reliable and the standard type of diversion in 1990s to which other types of diversion were compared [6]. The first attempt of ONB in human was performed by Lemoine in 1913. In this technique the two ureters were implanted in the rectum. Then the rectal segment was isolated and anastomosed to the urethra [5]. After that many advances in the techniques of ONB have been achieved till it become the most reliable and popular technique in males.

The encouraging results of orthotopic diversion in male raise the interest in applying the technique in women. However, this was not going on parallel with its application in men due to two main reasons. First, the available data on the natural history of synchronous and metachronous urethral involvement in Urothelial Carcinoma (UC) was limited before 1990. This is because the lower incidence of the disease in women in comparison to men together with the believes that the shorter female urethra is more close to the bladder neck and hence to the tumour. Thus cystourthrectomy was the standard of care in women [2]. Second; a little was known about the proper anatomical and functional features of female urethra and the settled disbelieves of the ability

Table 1: Incidence of continence and voiding problem after radical cystectomy and orthotopic diversion in women.

Reference	Patients No.	Daytime continence	Nocturnal continence	Chronic urine retention
Stenzl et al. [18]	102	82%	72%	12%
Ali-El-Dein et al. [19]	100	95%	86%	16%
Lee et al. [20]	53	87%	85%	21%
Granberg et al. [21]	49	90%	57%	35%
Stein et al. [22]	56	77%	77%	39%
Yang et al. [23]	56	60.4%	26.8%	24%
Anderson et al. [24]	49	57%	45%	31%
Jentzmik et al. [25]	121	82.4%	76.5%	58%

of shorter female urethra to maintain continence after cystectomy [7].

Many studies have been performed to revise the pathological features of UC specimens and the urethral involvement. These provided a scientific base for clinical application of USRC and ONB in women as long as there is no bladder neck involvement by the tumour [2]. Also, at the same times, several studies were performed to study the anatomical and functional behavior of female urethra which proved the ability to maintain continence with preservation of the distal two thirds of female urethra [7]. Now; we can confirm that with proper patient selection and refinement of surgical techniques, USRC and ONB in women has shown a comparable outcome to men.

Anatomy of Female Urethra and Continence Mechanism

An important cause of considering ONB for men and not in women was the believes that women would be unable to maintain continence after ONB. Therefore, urethrectomy was considered as an integral part of radical cystectomy in women [8]. This was changed after proper understanding of female urethral anatomy and continence mechanisms. In women, several factors can maintain continence at rest and at increased intra-abdominal pressure. The urethra is made of three functional structures that result in elastic, dynamic conduit with mucosal coaptation. The mucosa is formed of transitional epithelium with mucosal infoldings that allow distensibility and excellent coaptation. A sub mucosal spongy tissue made up of vascular networks. Surrounding the spongy tissue is a thin musculofascial envelope. These three components create a coaptive seal.

The female urethral sphincter is composed of smooth muscle sphincter and striated muscle sphincter (EUS). The smooth muscle sphincter is formed of inner longitudinal coat and a sparse outer semicircular coat. It is supplied by autonomic nerve supply from pelvic plexus composed mainly of cholinergic nerve endings and sparse adrenergic nerve ending. The striated muscle sphincter encircles the smooth muscle from the bladder base down to the perineum without distinction from urogenital diaphragm. It is more condensed around mid-urethra providing high pressure zone. It is innervated from below by the somatic fibers from pudendal nerve. The striated musculature (EUS) provides resting urethral tone as well as an involuntary reflex contraction in response to stress that increases coaptation. Adequate urethral length is essential to provide the coaptation for continence at rest and during increase in the abdominal pressure [9].

Both the bladder neck and the urethra are normally maintained in a high retropubic position relative to the more dependent bladder base, creating a valvular effect. Furthermore, intra-abdominal forces are directly transmitted to both bladder and proximal urethra.

It increases its resistance and promotes coaptation (pressure transmission hypothesis) [9]. De Lancey proposed the "hammock hypothesis" that abdominal pressure transmitted through the proximal urethra presses the anterior wall against the posterior wall. The posterior wall remains rigid if there is adequate pelvic support from muscle and connective tissues [10]. After anterior pelvic exenteration and excision of the whole vagina down just to below the bladder neck, good continent status is reported. However, most even all autonomic nerve supply is damaged [7].

Complete removal of the bladder neck with transaction of the proximal urethra just below the vesicourethral junction is safe because continence is maintained mainly by EUS. Therefore, with proper minimal dissection anteriorly along the pelvic floor to protect the pelvic floor musculature and the pudendal nerve to preserve the nerve supply to the EUS, postoperative continence should be maintained [11].

Patient's selection for orthotopic neobladder

Selection of female patients for ONB depends on three important factors. First is the oncological factor. Presence of bladder neck involvement, multifocal tumors, diffuse carcinoma *in situ*, clinically evident lymph node and distant metastasis are contraindication for USRC and ONB [12]. Second is the functional factor. Patients should be fully continent before surgery determined by proper history taking, pelvic examination, cystoscopy and urethral pressure profile [13]. Stenzl and Holtl had proposed specific criteria for predicting lower possibility of regaining postoperative continence in female. It included history of stress incontinence of grade II or more due to an incompetent sphincter, a marked urethral hypermobility or a maximal resting pressure in the UPP of less than 30 cm H₂O [7]. Also, good performance status is important as they need certain strength for continence training in the early postoperative period. Patients with ONB learn to void through simultaneous relaxation of the pelvic floor muscles and rising of intra-abdominal pressure with a valsalva maneuver. Third factor is the patients' motivation to undergo this surgery and accepting the related complication especially using Intermittent Self Catheterization (ISC) if Chronic Urine Retention (CUR) developed [7].

Voiding and continence outcome after RC and ONB

The main goal of ONB is to approximate the normal bladder function. The patient can void intentionally volitionally though the normal urethra. This to restore the preoperative function and maintain Health Related Quality Of Life (HRQOL). This clinically is achieved when neobladder allows volitional voiding four to six times daily (every 3 to 4 hours) with a capacity range of 400 to 500 ml of urine at low pressures [14].

Continence is influenced by accommodation of reservoir characteristics (large capacity, low pressure) as well as outlet resistance (continence mechanism). Ideal reservoir should achieve ideal functional, social, technical and safety criteria. From the functional point of view, it should be of adequate capacity to achieve accepted frequency of urine evacuation, durability, dryness and control without urge or stress. In addition, from the social point of view, it should preserve body image and provide day and night Continence. Furthermore, technically it should be feasible, with no need of foreign material, versatile to cope with different indications, allow surveillance of the upper tract as well as minimal need of revisional surgeries. Also, regarding safety of the reservoir, it is a critical point to be reviewed thoroughly before decision making. It should achieve safe resection from the digestive tract to minimize mal-absorption and diarrhea with less metabolic consequences. The reservoir should be Safe on the upper tract, with minimal risk of malignancies and with easy revisional surgery whenever indicated [15].

Continence problems

Urinary incontinence after ONB may develop due to pouch factors including: reduced capacity, high pressure, urinary tract infection, or presence of pouch stones. Also, loss of afferent input from the detrusor muscles to the central nervous system is thought to account, in part, for the worse continence at night in patients with an orthotopic substitute. Disturbance in the integrity of the external sphincter is the other factor that contributes to incontinence post orthotopic diversion. One contributing factor is thought to be worsening urethral sphincter function with age. Furthermore, decreased urethral sensitivity has been proposed as a potential factor contributing to urinary incontinence after radical cystectomy and orthotopic diversion [16].

Urodynamic evaluation of women with nocturnal incontinence post USRC and ONB revealed presence of pouch hyperactivity in 48% and reduced Maximal Urethral Closure Pressure (MUCP) and leak point pressure in (16%) of patients [17]. Recently, Gross et al. [13] reported that women with postoperative incontinence have lower functional urethral length (median 24mm vs. 32mm in continent women, $p < 0.001$) and lower postoperative urethral closure pressure (35cm H₂O vs. 56 cm H₂O, $p < 0.001$) at rest in comparison to continent women. Also, uterus preservation and trial of nerve sparing improved postoperative continence status [18].

The reported daytime continence after ONB in women ranged from 57% to 90%, while nighttime continence ranged from 27-86%. (Table 1).

Voiding problems

After ONB in women, not all women can void spontaneously. A considerable proportion of women develop Chronic Urine Retention (CUR). The incidence ranged between 12 to 58% of cases. (Table 1) Chronic Urine Retention (CUR) is defined as persistent inability to completely empty the pouch which results in elevated post voiding residual urine. According to our protocol, we advised patients to start ISC when post voiding residual urine is greater than 150 ml or more than 20% of the maximum reservoir capacity [19-25].

Till now the exact mechanism and cause of CUR after USRC and ONB is a matter of debate. There are two prevailing theories. The first theory explained it by autonomic denervation either completely causing a tonic proximal urethra that collapse during voiding causing obstruction or partially with sympathetic sprouting to denervated

smooth muscle sphincter causing obstruction. They recommended nerve sparing cystectomy to reduce the incidence of CUR [13,26]. However, denervation and urethral transection in dogs resulted in reduction of the pressure in the proximal urethra by 50% and did not affect the mid- or distal urethra and there was no detected fibrosis or collapse in the proximal urethra on cystoscopy [27].

The other theory postulated that the cause of CUR is a mechanical cause due to significant descent of the pouch and posterior pouch sagging with herniation through anterior vaginal wall during straining. This is based on the result of dynamic MRI and urodynamic investigation of women with CUR post USRC and ONB. The authors recommended mechanical modification to provide back support to the pouch [19].

Impact of continence problem on HRQOL

The advances in the field of UD were to improve patients' HRQOL. Orthotopic neobladder (ONB) was developed to deal with these concerns, enabling volitional voiding through the urethra and providing the additional advantage that a cutaneous stoma with the need for an external appliance is avoided [12].

Although many studies have discussed the impact of RC and UD on HRQOL, enough data in women is still lacking. Many studies reported no advantage of ONB over other form of diversion regarding patients' HRQOL [28-30]. On the other hand, Hobisch et al. [31] reported that ONB patients had better all domains of HRQOL in comparison to Ileal Conduit (IC) patients. Also, Philip et al. [32] reported more active life style and better HRQOL in ONB patients. However, the results of these studies needs proper interpretation due to small patients number and inclusion of both male and female patients. Only one recent study by Gacci et al. [28], compared HRQOL in women after different types of diversion and concluded that there was no statistically significant difference between IC and ONB.

Urinary troubles after UD have a significant impact on patients' HRQOL. Thulin et al. [33] reported that nocturnal incontinence affected patients' sleep and decreased their HRQOL than other diversion groups. This resulted in lower self-assessed HRQOL, physical health and energy level [33]. We compared the HRQOL of 74 women after RC and ONB with age matched normal group. There was statistically significantly lower all domains of HRQOL among the study group than the control group. The study group included 18 completely continent patients, 29 with nocturnal incontinence and 27 with chronic urinary retention. Completely continent women were comparable with those with chronic urinary retention. Women with night-time incontinence had a significantly worse HRQOL both groups [12].

Conclusion

Nerve sparing radical cystectomy and ONB has become the standard of care for selected women with muscle invasive bladder cancer. However, it is associated with significant incidence of continence and voiding problem that adversely affect patients' HRQOL. Proper patients' evaluation and identification of possible risk factors is mandatory before decision making in order to reduce the possible risk of continence trouble.

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