Surgery in Motion

Nerve-Sparing Radical Cystectomy and Orthotopic Bladder Replacement in Female Patients

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Abstract
Objectives: Orthotopic diversion, initially performed solely in men, has now become a viable option in women. Approximately 15 yr ago, at several centres, urethra-sparing cystectomy and orthotopic diversion were initiated in women with bladder cancer. Several studies have since addressed both the oncologic and functional outcomes of this procedure.

Methods: We describe our surgical technique of cystectomy and orthotopic urinary diversion in female patients, with an emphasis on how we preserve the neurovascular bundle.

Results and Conclusions: An improved understanding of the anatomic neurovascular and fascial planes related to the rhabdosphincter has facilitated identification of elements needed for orthotopic diversion in female patients. The technique of en bloc anterior exenteration includes the anterior portion of the vagina; however, preservation of the rhabdosphincter and its autonomic nerve supply necessitates specific modifications of the standard operation. The video provides a detailed description of our surgical technique with attention to anatomic details necessary to avoid damage to the proximal urethra and to preserve the autonomic innervation of the rhabdosphincter.

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1. Introduction
Radical cystectomy and lymphadenectomy is the most effective method for treating high-grade or invasive bladder cancer without evidence of systemic disease. In the 1980s, orthotopic reconstruction became the procedure of choice in selected male patients [1,2]. The excellent clinical and functional results achieved subsequently motivated an interest in applying orthotopic reconstruction to women [3]. This option is now possible because of an improved understanding of female pelvic anatomy as well as the substantiated low risk of urethral recurrence in women [4,5]. Specific pathologic criteria have allowed clinicians to select appropriate female candidates for orthotopic diversion. In addition, with the establishment of certain surgical modifications and the increasing availability of
clinical experience, a bladder substitute can now be offered to female patients.

Nerve-sparing cystectomy is equally as important in women as in men. The contribution to sphincter function of the intrapelvic pudendal somatic nerves and autonomic branches of the pelvic plexus has not been fully established, but animal studies have demonstrated a pressure increase in the distal urethra after pudendal nerve stimulation and in the proximal urethra after stimulation of the pelvic plexus [6]. This suggests that nerve sparing has functional significance for both continence and voiding ability. Using the female sheep model, Stenzl and colleagues found marked degeneration of the smooth muscles cells of the proximal urethra after bilateral denervation of an isolated urethra, which reflects the situation in patients with a bladder substitute [7]. Thereby complete autonomic denervation of the urethra in patients undergoing cystectomy and bladder substitute may result in long-term smooth muscle dysfunction. As reported, the absence of the tonus-regulating function of the autonomic nerves may lead to a dilation or rigidity of the urethra resulting in intrinsic sphincter deficiency. Intrinsinc sphincter deficiency has also been shown to result from hysterectomy due to urethral denervation from extensive pelvic dissection [8,9]. We believe that the denervated proximal urethra may result in ineffective active relaxation or kinking (or both) during voiding, and, thus, incomplete emptying that necessitates self-catheterisation.

The rhabdosphincter located in the middle and distal third of the female urethra technically permits proximal urethral excision en bloc with the cystectomy specimen. Stenzl and associates have reported excellent results in five women in whom 1 cm of proximal urethra was excised [10]. Despite this finding, we believe that the proximal urethra has functional significance. Urethral length is important in the genesis of urinary incontinence as demonstrated by the formula: continence = urethral length x closing urethral pressure [11]. In female sheep, Stenzl et al showed that maximal urethral closure pressure was markedly decreased in sheep with denervated urethra (18 cm H₂O compared to baseline of 49 cm H₂O) [7]. If the autonomic nerves are compromised, closing urethral pressure cannot compensate for a shortened urethral length. Theoretically, therefore, after resection of the proximal urethra, patients may not leak with increased intra-abdominal pressure because of the intact pudendal nerve pathway but may leak when they are walking, particularly if the bladder is full because of reduced functional urethral length. Also, sensory innervations of the proximal urethra may influence urinary continence. Division of these nerves may result in loss of the afferent limb of the external sphincter-guarding reflex stimulated by urinary leakage into the proximal urethra.

Other important considerations include preservation of the urethral support mechanism as well the vagina and uterus, but the desire to achieve functionally good results should not compromise the cancer operation. It is not uncommon for the primary tumour to involve the trigone. Coloby et al reported a 44% incidence in 43 cystectomy specimens in patients with transitional cell carcinoma [12]. There is no anatomic barrier, such as Denonvilliers fascia, between the bladder base and anterior vaginal wall. Lymphatic drainage from the bladder base and trigone occurs along the lateral vaginal wall to nodes along the hypogastric artery. Nerve sparing, though beneficial for voiding, is thereby only oncologically feasible when the risk of lymphatic spread and involvement is minimal. Accordingly, we excise the anterior vaginal wall with the specimen when invasive tumour is present in the bladder base or encroaches on the trigone.

Female nerve-sparing cystectomy and orthotopic bladder substitution is therefore complicated by the conflict between no violation of oncologic surgical principles and a functional neo-bladder with spontaneous optimal voiding. The compromise is extensive surgery on the tumour-bearing side and nerve sparing on the non–tumour-bearing side. Unfortunately, the finding of positive nodes only on the contralateral side to a lateralised bladder tumour occurs in up to 8% of patients with positive nodes and this must be discussed with the patient [13]. Additionally, female nerve-sparing cystectomy may affect sexual function; the parasympathetics maintain vaginal lubrication while other domains of sexual function are also affected.

2. Technical aspects

2.1. Patient preparation and incision

Patients eat a regular diet until the evening of surgery at which point they then consume only a light meal. Bowel preparation consists of two enemas late in the afternoon before day of surgery. Antegrade rinses of the bowel and neomycin-erythromycin intestinal preparations are avoided. Recent studies have found no significant difference in the rate of postoperative wound infections, clinical anastomotic leaks, or intra-abdominal abscesses between patients with and without antegrade bowel rinses [14,15]. Such preparations can
also increase the risk of fluid imbalances. In the elderly patient, this can produce cardiovascular instability due to intravascular volume depletion and can potentially place the patient in a catabolic state prior to surgery.

All patients receive perioperative and postoperative prophylactic antibiotics and subcutaneous heparin is administered in the arm the evening before surgery and continued postoperatively. Under general and epidural anaesthesia, the latter placed for postoperative pain control, the patient is placed in a dorsal Trendelenburg position with overextension of the pelvis for optimal exposure. The abdomen and vagina are then prepped and draped in the standard fashion. On the operative field, an 18F Foley catheter is introduced into the bladder. The approach is through a lower midline incision.

**2.2. Anterior exenteration in the female patient: lymphadenectomy**

A transperitoneal approach provides optimal access to the pelvic lymph nodes. In addition, the overlying round ligament needs to be dissected to obtain adequate exposure; the ovaries can be left in situ if they are normal appearing. An “extended” lymphadenectomy must include all lymph nodes in the boundaries of: the ureters crossing the common iliac artery and vein (proximally), the genitofemoral nerve (laterally), the circumflex iliac vein and inguinal ligament (distally), the hypogastric vessels (posteriorly), including the obturator fossa, presciatic nodes bilaterally, and the presacral lymph nodes anterior to the sacral promontory. To limit complications attributable to “extended” lymph node dissection, all afferent lymphatics from the lower extremities, which are transected, must be carefully ligated. We perform the lymphadenectomy before the cystectomy because this provides optimal exposure of the vascular supply to the bladder and uterus.

To initiate a pelvic lymphadenectomy, the peritoneum dorsal to the external iliac vessels is incised; this helps identify the vessels and dissection is then started lateral to the external iliac artery. The genitofemoral nerve coursing on the psoas muscle should be identified. The tissue over the external iliac artery and vein are divided and the dissection is carried down into the obturator fossa, which is cleared of all tissue with care to avoid injury to the obturator nerve. The obturator vessels are resected at their offspring from the internal iliac vessels and where they exit the pelvis. All connective, fatty, and lymphatic tissue is then removed from the lateral and medial aspect of the internal iliac vessels at the level of the promontory/S1/S2. Care must be taken not to injure the hypogastric nerves that run along the dorsolateral sigmoid/rectal wall. In patients at high risk for lymphatic spread, care is taken to clean out the fossa of Marcille, which is dorsolateral to the crossing of the common iliac vessels. Optimal access is obtained by mobilising and cleaning the proximal external iliac vessels away from the adjacent psoas muscle. On completion of the lymphadenectomy the pelvic wall is covered once again with the peritoneum.

3. **Cystectomy with uterine preservation**

The uterus can be spared if there is no invasive cancer in the area of the trigone or dorsal or lateral side walls of the bladder. The superior and inferior vesical arteries and veins are ligated and transected at their origin from the internal iliac vessels. The more distal vessels, which go to the paravaginal tissue and also the pelvic plexus, are left intact (Fig. 1). Because the uterus is being spared, the peritoneum is incised at the level of the uterovesical junction.

The bladder is mobilised along the anterior wall of the uterus. As the cervix is approached, the perivesical ureteral segments can be found. The junction between the cervix uteri and the anterior vaginal wall is then identified with the aid of a ring forceps in the vagina. It is essential to find the whitish plane on the outer surface of the vaginal wall on either side of the lateral wall of the cervix.

Fig. 1 – Female pelvic plexus anatomy.
Once this plane is identified, a Kelly clamp can easily be passed along the vaginal wall. On the side that a radical extensive resection of the dorsomedial bladder pedicle is required, the vaginal wall resection is dorsolateral, that is, at the 4 or 8 o’clock position (Fig. 2). In doing so, the paravaginal tissue containing autonomic nerves, which run to the proximal sphincter, are inevitably resected. Remaining in close contact with the whitish wall of the vagina ensures that the paravaginal venous plexus is hemostatically controlled and resected with the dorsomedial bladder pedicle.

On the side of attempted nerve sparing, the vaginal wall dissection at the cervical level is in the anteroventral plane of the vagina, that is, at the 2 or 10 o’clock position (Fig. 2). In addition the dorsomedial pedicle is transected close to the bladder wall. Once the trigone is approached, it is imperative to dissect close to the bladder neck.

After transecting the paravaginal dorsomedial bladder pedicle to the bladder neck, the Foley balloon in the mobile bladder is easily palpated and both sides of the vesicourethral junction can accordingly be identified. At the level of the bladder neck, the endopelvic fascia is incised transversely. Venous bleeding ventral to the urethra is controlled with sutures or by the suction device so as to provide optimal visualisation of the proximal urethra. We feel that it is important to incise the endopelvic fascia close to the bladder neck, thereby avoiding injury to the paraurethral structures (urethral support, vascular supply, innervation). The urethra itself should be sharply divided approximately 5 mm distal to the vesicourethral junction. Thereby, the urethral functional length is only reduced to approximately 24–27 mm and the benefits of preserving at least part of the proximal urethra have previously been discussed.

4. Cystectomy without uterine preservation

Essentially, the technique is similar to that described above. However, in this case the peritoneum is incised in the Douglas cavity just below the vaginal fundus whose location is made visible by a ringed forceps in the vagina. When dissecting caudally along the vagina it is again essential to find the whitish plane on the outer vaginal wall. The dorsomedial bladder pedicles are transected as described above. On reaching the vesicourethral junction (bladder neck), the vagina is opened circumferentially close to the dorsal surface of the cervix. The anterior wall is then palpated with the surgeon’s finger. Since the paravaginal tissue was previously ligated with the dorsomedial pedicle of the bladder, the vaginal wall covering the trigone can now be excised without significant blood loss. If tumour location permits then the caudal resection of the anterior vaginal wall should be approximately 1 cm cephalad to the urethral resection plane. This manoeuvre prevents the vaginal wall sutures from laying directly under the anastomotic sutures between the reservoir and urethra and thereby decreases the risk of a vesicovaginal fistula. A fistula risk is further minimised if electrocautery use is avoided so as to preclude thermal injury to the tissue borders required for approximation.

The vaginal wall is closed transversely by folding the pouch of Douglas down to the caudal resection line along the anterior vaginal wall. Running Vicryl 2-0 suture is used to close the vagina with care to evert the vaginal epithelium towards the vagina to prevent lip fistulas. The peritoneum that covers the
posterior vaginal wall is thereafter pulled over the suture line and fixed to the periurethral fascia in front of the anterior vaginal wall where the urethra has been resected.

5. **Orthotopic bladder substitute**

5.1. *Preparation of the ileal segment for the bladder substitute*

The orthotopic bladder substitute is performed by isolating 55 cm of ileum, 25 cm proximal to the ileocecal valve (Fig. 3). The ileocecal valve and the most distal 25 cm of ileum are preserved to reduce the risk of associated malabsorption and steatorrhea. One hour prior to reservoir construction, administration of analgesic/local anaesthetic mixture via the epidural is ceased. This prevents increased muscle tone and activity that would result in an artificial shortening of bowel and thereby the potential to remove too much bowel for pouch reconstruction. The ileum used for bladder substitute construction is then measured with a 10-cm ruler along the mesoileum and without overstretching of the bowel.

The distal mesenteric division, which is essential for adequate mobility of the reservoir, should extend deep into the mesentery. The proximal mesenteric division, however, is short and ensures a broad vascular blood supply to the bladder substitute by at least two separate vascular arcades. To re-establish bowel continuity, a small-bowel anastomosis is performed end-to-end with a running (4-0 Vicryl) suture through the seromuscular layers. This same technique is used for closure of both ends of the ileal segment. The mesenteric gap is then closed.

The harvested ileum is divided between the proximal afferent segment and the distal 42–44-cm segment that will form the reservoir of the bladder substitute. This distal part of the ileal segment is opened with scissors along the antimesenteric line (Fig. 4).

5.2. *Ureteroileal anastomosis*

The left ureter is mobilised up to the lower pole of the kidney with care to maintain its surrounding blood supply and thereby prevent ischemia. It is then brought without tension to the right side of the abdomen retroperitoneally by crossing the aorta slightly above the inferior mesenteric artery. Note that if the ureters need to be resected close to the kidney (carcinoma in situ, compromised vascular supply, previous radiation history), a longer afferent ileal segment can be harvested to bridge the necessary distance.

The ureters are anastomosed in an end-to-side fashion to the proximal (non-incised) afferent tubular portion of ileum. The ureteral ends are then spatulated over a length of 2 cm. The anastomoses are placed paramedial to the antimesenteric border at the most proximal portion of the afferent tubular segment. To prevent ischemia of the bowel between the ureteral anastomoses, the right ureter is placed approximately 1 cm distal to the left ureter.

After placing a suture (4-0 polyglycolic acid) at each end of the spatulated ureter and ileal incision, the anastomosis is performed using the Nesbit technique. To prevent a fistula resulting from ure-
teral mucosa prolapse and to establish a watertight anastomosis, special attention should be made to have the ureteral wall lie between the mucosa and seromuscular layer of the bowel. This is accomplished by starting each anastomosis on the ureteral wall. At the proximal angle, with running 4-0 Vicryl suture, a minimal amount of ureteral tissue is anastomosed to the seromuscular layer of bowel so as to prevent narrowing of the ureter. Gradually the amount of ureteral tissue incorporated increases to secure the anastomosis.

Prior to completion of the anastomoses each ureter is stented with an 8F ureteral catheter that is secured with 4-0 Rapid Vicryl through the wall of the ureter and stent and loosely tied so as to prevent ischemia. Tension on the anastomosis is avoided with three interrupted sutures placed between the distal periureteral tissue and the afferent tubular segment. By doing so, the periureteral tissue also covers the suture line. The stents are then passed through the distal tubular segment wall where their exit sites are covered with mesenteric fat to prevent leakage of urine when they are eventually removed (Fig. 5).

5.3. Bladder substitute construction

The previously opened portion of the ileal segment is folded into a U shape and the two medial borders are sewn together at the seromuscular layers with running 2-0 Vicryl suture as shown in Figs. 4 and 6. The bottom of the U is folded up between the two sides of the U forming a sphere-shaped reservoir (Fig. 6). This effectively creates a low-pressure spherical-shaped reservoir with an initial capacity of approximately 120 ml. Prior to final closure of the reservoir, the surgeon’s forefinger is introduced to determine its most dependent part and a 1-cm diameter hole is excised from the wall as shown in Fig. 7. Although it may appear easier to perform, it is imperative that the anastomosis of the urethra to the neo-bladder is not to the funnel-shaped end of the reservoir. This error would increase the risk of kinking and obstruction at the anastomotic site (Fig. 8). To achieve optimal voiding, the anastomosis must sit broadly on the pelvic floor.

Fig. 5 – Ureteroileal anastomosis.

Fig. 6 – Bottom of the U is folded up between the two sides of the U.

Fig. 7 – Surgeon’s finger is introduced to determine the most dependent part and a 1-cm diameter hole is excised.
After a silicone 18F Foley urethral catheter is placed, six 2-0 Vicryl sutures anastomose the previously made hole in the neo-bladder with the urethra (Fig. 9). The two posterior sutures are anchored to the periurethral fascia overlying the anterior vaginal wall, two laterally through the urethra and then two anterior sutures at 1 and 11 o’clock are anchored to the endopelvic fascia. When placing the urethrointestinal sutures, the needle incorporates 3–4 mm of the sphincter but exits at the mucosal edges, thereby bringing the two mucosal edges close together and maximising urethral length as well as reducing the incidence of anastomotic strictures. If necessary, the operating table is now flexed to reduce the distance between the bladder substitute and the urethra. In situations where the mesentery is short and the anastomosis between the reservoir and urethra is under tension, careful superficial incisions of the bladder substitute mesentery will provide for further length. Sutures are loosely tied to prevent cutting, ischemia, and stenosis. Before complete closure of the reservoir, a cystostomy tube is passed through the neo-bladder wall where its exit site is covered with mesenteric fat (Fig. 10). The cystostomy tube provides assurance of adequate reservoir drainage during the healing phase, precluding overdistention or rupture of the suture lines in case the indwelling urethral catheter becomes obstructed. Rarely do we place omentum between the reservoir and vaginal wall; it is necessary only if no other tissue can be placed between the vaginal suture line and the sutures anastomosing the reservoir and urethral stump. If the anterior wall of the reservoir has the potential to protrude in front of the bladder outlet with voiding, then it should be fixed to the symphysis with a single suture. However, this should not be a suspension suture. A pouchocèle is ideally prevented by leaving the uterus in situ and asking the patients to not strain with voiding. In our experience, some patients postoperatively have inadequate relaxation of the urethra with failure to open the urethra with voiding and subsequently develop a cystocele. In our opinion, cystoceles are rather a consequence of women straining to void against a dysfunctional urethra and rarely the primary etiology of impaired voiding. However, once a cystocele develops, voiding becomes increasingly difficult with the additional kinking of the angle between the reservoir and urethra.

Fig. 8 – Anastomosis of the urethra to the neo-bladder is not made to the funnel-shaped end of the reservoir.

Fig. 9 – Six 2-0 Vicryl sutures anastomose the previously made hole in the bladder substitute to the urethra.
6. Postoperative care

Critical components to good long-term results require not only surgical finesse but also patient compliance and meticulous postoperative care. Ureteral stents are removed 4–7 d after surgery. At 8–10 d postoperatively and after a pouchography documents no evidence of urinary leakage, the cystostomy tube is removed. The Foley catheter remains for an additional 2 d to provide adequate time for closure of the cystostomy tube exit site from the bladder substitute wall. Although our patients are receiving antibiotics, all drains are removed as early as possible to prevent infections. After the patient is drain free, any bacteriuria is treated with antibiotics until the urine is sterile.

Patients are carefully instructed on how to void. Initially, they are taught to empty the neo-bladder every 2 h during the daytime in a sitting position by relaxing the pelvic floor and increasing the intra-abdominal pressure. At night, they are instructed to use an alarm clock to void every 3–4 h. Initially, the urine is often hyposmolar and consequently, the neo-bladder will secrete sodium chloride, resulting in a salt-losing syndrome and thereby hypovolaemia and metabolic acidosis. To prevent this series of metabolic events, patients are instructed to consume 2–3 l of fluids a day and to increase salt intake. With time, the villi will atrophy and this syndrome will become less pronounced. These patients are carefully followed with regular assessments of blood gases and body weight.

Patients without metabolic acidosis (no negative base excess) or those managed appropriately with oral sodium bicarbonate are instructed to retain urine for 3 h and later for 4 h to obtain a bladder capacity of up to 500 ml. During this exercise, increased neo-bladder pressures may result in incontinence, but the elevated pressures are essential to increase the reservoir’s capacity. Therefore, patients are advised to not void when they experience such incontinence; otherwise the neo-bladder will never achieve the desired capacity.

With increasing capacity, nighttime continence will improve but, on the other hand, a neo-bladder capacity of >500 ml should be prevented. Over-distention of the reservoir will result in a floppy pouch unable to adequately empty, increased residual urine, and the potential for urinary retention. Residual urine should be monitored, recognised early, and promptly managed. The most common reasons for residual urine are protrusion of ileo-bladder mucosa into the urethra and urethral anastomotic strictures. Both of these can be managed endoscopically. Permanent indwelling catheters and intermittent straight catherisations are not adequate therapies and are reserved only for patients for personal preferences or for nursing purposes. In addition, bacteriuria should also be appropriately treated. Our patients are followed regularly at every 6 mo for 5 yr and then at yearly intervals.

7. Conclusion

Traditionally, anterior exenteration for transitional cell carcinoma necessitated performance of a total urethrectomy and therefore orthotopic diversion was thought not feasible in women. Recently, however, investigators have reported a low rate of urethral involvement (<2%) in female patients with bladder cancer [5]. Of more importance, however, is the likelihood of pelvic recurrence because of attempted nerve or genital organ sparing. Therefore, bilateral nerve sparing is rarely possible.

The autonomic nerve fibres are particularly at risk at two points: where they pass medial to the ureters and lateral to the cervix, that is, where they
cross the uterine and vaginal arteries, and in the paravaginal/bladder neck area. We advocate nerve-sparing radical cystectomy, at least on one side, if oncologically feasible because of the voiding advantages discussed previously and because preservation of the autonomic nerves is essential to preserve lubrication of the vagina. A well-lubricated vagina is much more important than its functional length. A somewhat shorter but well-lubricated vagina allows for normal intercourse; however, a long narrow dry vagina will not.

Data concerning the effect of nerve-sparing radical cystectomy on sexual function is rare. The impact of non–nerve-sparing cystectomy on female sexual function has been previously reported by Volkmer et al and by Zippe et al, with both groups showing a decrease in multiple domains postoperatively [16,17]. In a recent investigation, sexual function was preserved in patients who received neurovascular preservation, whereas multiple domains of sexual function declined in patients who had undergone non-neurovascular preservation [18]. However, these results are hampered with additional hysterectomies performed in the non–nerve-sparing group as well as a small sample cohort size.

A successful functional outcome may be achieved in women after bladder substitution [19]. However, it is imperative that the radical nature of cancer surgery not be compromised by the orthotopic reconstruction.

**Conflicts of interest**

The authors have nothing to disclose.

**Appendix A. Supplementary data**

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.eururo.2007.02.048 and via www.europeanurology.com. Subscribers to the printed journal will find the supplementary data attached (DVD).

**References**