Orthotopic Ileal Bladder Substitution in Women: Factors Influencing Urinary Incontinence and Hypercontinence

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Abstract

**Background:** Urinary incontinence or the inability to void spontaneously after ileal orthotopic bladder substitution is a frequent finding in female patients.

**Objective:** To evaluate how hysterectomy and nerve sparing affect functional outcomes and whether these relate to pre- and postoperative urethral pressure profile (UPP) results.

**Design, setting, and participants:** Prospectively performed pre- and postoperative UPPs of 73 female patients who had undergone cystectomy and bladder substitution were correlated with postoperative voiding and continence status.

**Outcome measurements and statistical analysis:** Outcome analyses were performed with the Kruskal-Wallis test, Wilcoxon-Mann-Whitney, or two-group post hoc testing with the Bonferroni correction. Chi-square or Fisher exact tests were applied for the categorical data.

**Results and limitations:** Of postoperatively continent or hypercontinent patients, 22 of 43 (51.2%) had the uterus preserved; of incontinent patients, only 4 of 30 (13.3%, \( p < 0.01 \)) had the uterus preserved. Of postoperatively continent or hypercontinent patients, 27 of 43 patients (62.8%) had bilateral and 15 of 43 (34.9%) had unilateral attempted nerve sparing. In incontinent patients, 11 of 30 (36.7%) had bilateral and 16 of 30 (53.3%) had unilateral attempted nerve sparing (\( p = 0.02 \)). When compared with postoperatively incontinent patients, postoperatively continent patients had a longer functional urethral length (median: 32 mm vs 24 mm; \( p < 0.001 \)), a higher postoperative urethral closing pressure at rest (56 cm H\(_2\)O vs 35 cm H\(_2\)O; \( p < 0.001 \)) as well as a higher preoperative urethral closing pressure at rest (74 cm H\(_2\)O vs 47.5 cm H\(_2\)O; \( p = 0.01 \)). The main limitation was the limited number of patients.

**Conclusions:** In female patients undergoing radical cystectomy and bladder substitution, preservation of the uterus and attempted nerve sparing results in better functional outcomes. The preoperative UPPs correlate with postoperative voiding and continence status and may predict which patients are at a higher risk of functional failure after bladder substitution.

**Patient summary:** If preservation of the urethra's innervation is not possible during cystectomy, poor functional results with bladder substitutes are likely.

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1. Introduction

Urinary incontinence and the inability to completely void spontaneously (“hypercontinence”), or a combination thereof, are observed in up to 50% of women after ileal orthotopic bladder substitution (BS) following radical cystectomy (RC) [1]. This rate is much higher than that following ileal bladder augmentation procedures that leave intact the sphincter apparatus and the bladder neck and its innervation [2]. We examined the possible effects of hysterectomy [3] (prior or simultaneous) and attempted nerve-sparing cystectomy on postoperative functional outcomes in women with a bladder substitute, whether pre- and postoperative urethral pressure profile (UPP) findings correlated with them, and whether preoperative UPP findings can predict functional outcomes.

2. Patients and methods

A total of 73 female patients (median age: 61.7 yr; range: 34.7–78.5 yr) were included in the study. Four of the women (5.5%) underwent RC for postirradiation cystitis and 69 for invasive urothelial cancer [4] (Table 1). All patients were preoperatively continent or experienced occasional dropwise urinary incontinence and were able to void spontaneously. Hysterectomy had been performed previously in 16 patients (21.9%) and at the time of RC in 31 (42.5%). Nerve sparing was attempted bilaterally in 38 patients (52%) and unilaterally in 31 (42.5%) as described previously [5]. In four patients (5.5%) no nerve sparing was possible due to extensive disease.

After surgery all patients had a cystogram before catheter removal between postoperative days 10 and 12. They were instructed on how to void the bladder substitute by relaxing the pelvic floor and exerting only minimal abdominal straining. All patients were followed up at 3-mo intervals during the first postoperative year, biannually up to 5 yr, and at least once a year thereafter [6]. Any bacteriuria with \( \geq 10^5 \) germs was treated. Residual urine was measured by transabdominal ultrasound or by in-and-out catheterisation. To determine whether there was any mechanical outlet obstruction, patients with documented postvoid residual urine (PVR; > 50 ml) underwent urethrocystoscopy with a rigid endoscope. After filling the bladder substitute, the endoscope with its mechanical outlet obstruction, patients with documented postvoid residual urine (PVR; > 50 ml) underwent urethrocystoscopy with a rigid endoscope. After filling the bladder substitute, the endoscope with its outlet valve open was retracted to the proximal urethra to determine whether there was prolapsing mucosa or a kinking of the proximal urethra resulting in a mechanical outlet obstruction while the bladder substitute emptied. Urinary continence and pad use were assessed prospectively at 6-mo intervals in all patients using previously published questionnaires [7]. The use of one or no safety pad per 24 h was classified as continent. Patients with a reservoir capacity < 300 ml (known possible cause for incontinence) were excluded from the analysis, as well as three patients who were continent but had a mechanical outlet obstruction (mucosal prolapse, urethral stricture) [8].

2.1. Urethral pressure profiles

UPPs were performed prospectively before RC and BS and at various intervals thereafter with the patient’s consent. Urinary incontinence was excluded by dipstick, microscopic examination of urine sediment, and urine culture. Any urinary infection (\( \geq 10^6 \) germs) was treated according to antibiogram before UPP was performed. Before UPP examination the bladder substitute was first evacuated by a disposable catheter; hypercapacity was excluded. In patients with PVR, a micturition cystogram was performed. In a lithotomy position, a T-DOC-7FD 7F air-charged dual-sensor catheter (T-DOC, Wilmington, DE, USA) was placed, and the bladder substitute was filled with 50 ml isotonic saline. UPP recordings were made with a Laborie Triton multichannel urodynamic system (Laborie, Toronto, Canada). The dual-sensor catheter was pulled twice from the bladder substitute to the external meatus at a rate of 1 cm/s.

All UPP results were reevaluated by a single expert (T.G.). The continence product was calculated by multiplying the functional urethral length by the maximal urethral closing pressure at rest [9].

Overall, 60 of the 73 patients underwent both pre- and postoperative UPP at rest; 13 did not undergo preoperative UPP. For every patient, the preoperative UPP (if available), the first postoperative UPP, and only the first UPP when the final voiding and continence status was reached were analysed. Several patients with perfect bladder substitute function did not consent to repeat postoperative UPP examinations, accounting for the rather small number of evaluated continent patients.

The patients were divided into four groups based on the final postoperative clinical findings. Group 1 was continent with spontaneous voiding and no PVR (n = 36). Group 2 was continent with spontaneous voiding and no PVR (n = 17). Group 3 wascontinent with PVR (n = 13). Group 4 was continent with PVR and no mechanical outlet obstruction (n = 7).

In the 60 patients with both pre- and postoperative UPPs, the final postoperative continence and voiding status was compared with the preoperative UPP results. The study was approved by the local ethics committee (E19-12-13).

2.2. Statistical analysis

The continuous variables are described with median and range. Categorical data are presented as counts or percentages. For comparison

Table 1 – Patient characteristics

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continent, no PVR</td>
<td>Incontinent</td>
<td>Continent with PVR</td>
<td>Incontinent</td>
<td>Continent with PVR</td>
</tr>
<tr>
<td>Age at surgery, yr, median (range)</td>
<td>61.5 (34.7–78.5)</td>
<td>64.2 (54–76.8)</td>
<td>62.1 (53.6–77.9)</td>
<td>52.7 (37.6–63.8)</td>
</tr>
<tr>
<td>Overall follow-up, mo (range)</td>
<td>65 (12–227)</td>
<td>46 (12–171)</td>
<td>120 (12–144)</td>
<td>33 (12–180)</td>
</tr>
<tr>
<td>Time to UPP when final voiding/continence status was reached, mo, median (range)</td>
<td>3 (3–72)</td>
<td>6 (3–12)</td>
<td>12 (3–84)</td>
<td>10 (8–12)</td>
</tr>
<tr>
<td>Tumour stage, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pT0</td>
<td>1 (2.8)</td>
<td>0 (0)</td>
<td>2 (15.4)</td>
<td>1 (14.3)</td>
</tr>
<tr>
<td>pT1</td>
<td>10 (27.8)</td>
<td>3 (17.7)</td>
<td>3 (23.1)</td>
<td>1 (14.3)</td>
</tr>
<tr>
<td>pT2</td>
<td>12 (33.3)</td>
<td>10 (58.8)</td>
<td>2 (15.4)</td>
<td>4 (57.1)</td>
</tr>
<tr>
<td>pT3</td>
<td>10 (27.8)</td>
<td>4 (23.5)</td>
<td>6 (46.1)</td>
<td>1 (14.3)</td>
</tr>
<tr>
<td>pT4</td>
<td>3 (8.3)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

PVR = postvoid residual urine; UPP = urethral pressure profile.
of independent groups, the Kruskal-Wallis test was used for continuous
test was used if only two groups
were compared. If the Kruskal-Wallis test result was significant, two-
post hoc testing with the Bonferroni correction for multiple
testing was performed. The chi-square or the Fisher exact test was
applied for the categorical data.

3. Results

3.1. Hysterectomy

Of postoperatively continent patients (groups 1 and 4), 51.2% had the uterus preserved; of incontinent patients (groups 2 and 3), only 13.3% did (p < 0.01) (Fig. 1).

Patients with a preserved uterus postoperatively had a longer functional urethral length (median: 30 mm vs 27 mm; p < 0.01), a higher maximal urethral closing pressure at rest (median: 55.5 cm H\textsubscript{2}O vs 44 cm H\textsubscript{2}O; p < 0.01), and a higher continence product (median: 1589 cm H\textsubscript{2}O × mm vs 1200 cm H\textsubscript{2}O × mm; p < 0.001) than hysterectomised patients.

Women with a preoperative hysterectomy had preoperatively a significantly lower maximal urethral closing pressure at rest (median 56.5 cm H\textsubscript{2}O vs 65.5 cm H\textsubscript{2}O; p < 0.01) and a continence product (median: 1589 cm H\textsubscript{2}O × mm vs 1200 cm H\textsubscript{2}O × mm; p < 0.001) than women without a preoperative hysterectomy.

3.2. Nerve sparing

In the postoperatively continent patients (groups 1 and 4), nerve sparing was attempted bilaterally in 62.8% and unilaterally in 34.9%, whereas in incontinent patients (groups 2 and 3), bilateral nerve sparing was attempted in 36.7% and unilateral in 53.3% (p = 0.02) (Fig. 2). Patients with bilateral nerve sparing had the highest continence product (1470 cm H\textsubscript{2}O × mm); the four patients without had the lowest (840 cm H\textsubscript{2}O × mm).

3.3. Postoperative urethral pressure profile findings at rest at the time of final continence and voiding status

Postoperatively incontinent patients without PVR (group 2) had a significantly shorter functional urethra compared with continent patients without PVR (group 1) (median 24 mm vs 30 mm; p < 0.001) and a significantly lower median maximal urethral closing pressure at rest (median 39 cm H\textsubscript{2}O vs 53 cm H\textsubcript{2}O; p < 0.001) (Fig. 3), with a consequently significant difference in the continence product (Table 2).

The UPPs of incontinent patients with PVR (group 3) revealed a similarly short urethral length (26 mm vs 24 mm) and tended to have a lower median maximal urethral pressure at rest compared with UPPs of incontinent patients without PVR (group 2) (28 cm H\textsubscript{2}O vs 39 cm H\textsubscript{2}O; p = 0.7). At endoscopy either their urethra did not open when they were asked to void or the hypotonic proximal urethra acted as a flap valve (Fig. 4) [10].

The UPPs of continent patients with PVR (group 4) when compared with those of continent patients without PVR (group 1) showed a longer urethral length (median: 35.5 cm vs 30 mm; p = 0.06), a significantly higher median maximal urethral pressure at rest (median: 81.5 cm H\textsubscript{2}O vs 53 cm H\textsubscript{2}O; p = 0.01), and a significantly higher continence product (p = 0.002) (Table 2). At urethroscopy a tight proximal urethra was seen in these patients (Fig. 5) [10]. The early postoperative UPP findings resemble those of the final postoperative UPPs but with lower median values (data not shown).

3.4. Preoperative urethral pressure profile and final postoperative continence status

Postoperatively continent patients (groups 1 and 4) had a longer preoperative functional urethral length (medians: 35 mm and 40 mm, respectively) compared with postoperatively incontinent patients (groups 2 and 3) (median: 32 mm and 31.5 mm, respectively; p = 0.08) (Table 3). Postopera-
tively continent patients (groups 1 and 4) had significantly higher preoperative maximal urethral closing pressures at rest and continence product than did postoperatively incontinent patients (groups 2 and 3) (Fig. 6; Table 3).

Postoperatively continent patients with PVR (group 4) had preoperatively a significantly higher continence product compared with postoperatively continent patients without PVR (group 1) (Table 3).

### 3.5. Continent patients who built up postvoid residual during follow-up

The seven continent patients with PVR (group 4) were first able to void without PVR in the early postoperative period. Their early postoperative UPP showed a decrease in functional urethral length (from a median of 40 mm preoperatively to 30 mm postoperatively), a decrease in maximal urethral closing pressure at rest (from a median of 94 cm H₂O preoperatively to 60 cm H₂O postoperatively), and a decrease in continence product (from a median 3620 cm H₂O x mm preoperatively to 1725 cm H₂O x mm postoperatively). After an increase in PVR between months 3 and 6 postoperatively, these patients exhibited an increase in functional urethral length (from a median 30 mm to 35.5 mm), a significant increase in maximal urethral closing pressure at rest (from a median 60 cm H₂O to 81.5 cm H₂O; p = 0.01), and an increase in the continence product (from a median 1725 cm H₂O x mm to 2610 cm H₂O x mm; p < 0.001) compared with the early postoperative UPP results.

Two patients with postoperative hypertonic urethra (group 4) were able to void spontaneously without PVR after transurethral incision/resection of the most proximal part of the urethra.

![Fig. 2](image2.png)  
**Fig. 2** – Incidence of attempted nerve-sparing cystectomy in continent patients with and without postvoid residual (PVR) (groups 1 and 4) and incontinent patients with and without PVR (groups 2 and 3). PVR = postvoid residual urine.

![Fig. 3](image3.png)  
**Fig. 3** – Median maximal urethral closing pressure at rest at the time of final postoperative continence and voiding status. PVR = postvoid residual urine.

![Fig. 4](image4.png)  
**Fig. 4** – Endoscopic finding of a denervated hypotonic proximal urethra that acts like a flap valve (arrow) when voiding. Patients with this finding were incontinent and unable to void to completion.
3.6. Patients whose continence status changed postoperatively

Twelve patients who were incontinent without PVR in the early postoperative period became continent without PVR during follow-up. When comparing their early postoperative UPPs with later ones when they were continent, a significant increase in functional urethral length, maximal urethral closing pressure at rest, and continence product (from a median 600 cm H$_2$O/C$_2$mm to 1568 cm H$_2$O/C$_2$mm; $p < 0.001$) were found (Fig. 7).

One patient was initially continent without PVR (group 1) and then became incontinent without PVR (group 2) after pelvic tumour recurrence. Her UPP showed a decrease in functional urethral length (from 27 mm to 18 mm), a decrease in maximal urethral closing pressure at rest (from 55 cm H$_2$O to 31 cm H$_2$O), and a decrease in continence product (from 1485 cm H$_2$O/C$_2$mm to 558 cm H$_2$O/C$_2$mm).

4. Discussion

In addition to the radicality of surgery, the main challenge of RC and BS is optimising the functional outcome. BS in women results in higher percentages of incontinence and...
PVR than in men [11,12]. Our present results show a strong correlation between postoperative urinary incontinence and pre- or perioperative hysterectomy, attempted nerve sparing, and the pre- and postoperative UPP findings. These findings suggest that voiding disorders after BS in women are related to whether the autonomic nerves to the female urethra (which run closely along the lateral aspect of the cervix uteri) are preserved or damaged. The autonomic nerve fibres coming from the pelvic (inferior hypogastric)
plexus innervate almost exclusively the proximal third of the female urethra and, to a lesser extent, the middle third of the urethra [13]. The sympathetic nerves are mainly responsible for urethral tonus at rest and assuring urinary continence [14]. The parasympathetic fibres activate the detrusor and trigonal area for initiation of voiding and counteract the sympathetic influence on the sphincter detrusor and trigonal area for initiation of voiding and threshold and is often associated with urinary incontinence, reflex) responsible for sensory neurofeedback (eg, the guarding continence responsible for urethral tonus at rest and assuring urinary success) cystocele formation undertook surgical measures to avert (usually without collapsing urethra) should be prevented rather than 

Our findings regarding postoperative urinary incontinence accord well with the known neurophysiology and with reports on the beneficial effect of nerve-sparing surgery on urinary incontinence in male patients after radical prostatectomy [19,20]. Incontinent patients have a significantly lower urethral tonus at rest and also a shortened functional urethral length. A completely denervated atonic proximal urethra does not remain a rigid tube or open conduit, but its walls collapse when voiding. As a result, the patient is not only incontinent but is not able to void without PVR. Such patients have the poorest continence product of all female patients with postoperative voiding disorders after BS (Table 2).

Interesting are the findings in 12 of our patients who were initially incontinent without PVR (suggesting non-total denervation of the most proximal urethra without consecutive atrophy and kinking) and became continent upon longer follow-up. The functional length of the urethra increased significantly from 21 mm when they were incontinent to 30 mm when they became continent. At the same time, the maximal urethral closing pressure at rest increased significantly from 30 cm H₂O to 50 cm H₂O, that is, to values of patients who were continent from the early postoperative period on (Fig. 7). Recovery from neuropaxia is the most likely cause of these findings because both the functional length and the maximal urethral closing pressure at rest increased significantly over time.

A converse finding was noted in a patient who became incontinent with a parallel decrease in functional urethral length and maximal urethral closing pressure at rest when she developed a pelvic recurrence, suggesting infiltration of the autonomic nerves to the urethra.

A cystogram was performed in all our patients postoperatively, and no cystoceles were found in any patient. However, if a patient could only empty the bladder substitute by straining, cystoceles were documented. Cystocele formation therefore was not the cause of PVR but rather a consequence of an outlet obstruction (functional or mechanical) obliging the patient to strain when voiding. Thus the formation of mechanical and functional outlet obstructions (by kinking of a funnel-shaped reservoir outlet or of a denervated proximal collapsing urethra) should be prevented rather than undertaking surgical measures to avert (usually without success) cystocele formation [21].

The present findings also allow characterisation of another specific form of dysfunctional voiding, namely perfect urinary continence with PVR. These patients were found to have a hypertonic urethra with very high maximal urethral closing pressures at rest of approximately 80 cm H₂O. Usually these patients were continent and able to void immediately after surgery, but 3–6 mo later they started to build up residual urine and complain about voiding difficulties. At that time their UPPs were higher than they had been immediately after surgery but still lower than before surgery. This leads us to assume that they are unable to relax the proximal part of the urethra due to intraoperative damage to parasympathetic nerves and its over-stimulation by sympathetic nerves. It is noteworthy that female patients who remained continent after BS (groups 2 and 3) already had a lower median continence product preoperatively compared with postoperatively continent patients (groups 1 and 4).

It is a limitation of this study that the number of patients examined was too small to allow definition of clear-cut limits to the preoperative continence product, but if values are <1600 cm H₂O × mm, the risk for postoperative incontinence is known to be high (79% in our population). Furthermore, other factors may contribute in whole or in part to postoperative incontinence. In addition to prior or concomitant hysterectomy, attempted nerve-sparing surgery, age, and urinary infection, surgical factors may also play a role. If the urethra is cut too short or injured in other ways (such as thermal injury), even the best performed nerve-sparing procedure may not prevent postoperative urinary incontinence after BS. Conversely, if the preoperative continence product is >3000 cm H₂O × mm, the risk of incomplete voiding is high (50% in our population).

5. Conclusions

After RC and BS in women, postoperative continence status correlates with the pre- and postoperative UPP findings. Significantly better functional outcomes are achieved when preservation of the uterus and nerve sparing are attempted. If, however, the preoperative continence product is <1600 cm H₂O × mm or >3000 cm H₂O × mm, postoperative urinary incontinence or the inability to void is likely, and the patient should be informed accordingly.

Author contributions: Urs E. Studer had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Ruf, Studer.
Acquisition of data: Gross, Ruf, Meissner, Ochsner.
Analysis and interpretation of data: Gross, Studer.
Drafting of the manuscript: Gross.
Critical revision of the manuscript for important intellectual content: Meissner, Studer.
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Obtaining funding: None.
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Supervision: Studer.
Other (specify): None.
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References