Readaptation of the Peritoneum Following Extended Pelvic Lymphadenectomy and Cystectomy Has a Significant Beneficial Impact on Early Postoperative Recovery and Complications: Results of a Prospective Randomized Trial

Beat Roth, Frédéric D. Birkhäuser, Pascal Zehnder, Fiona C. Burkhard, George N. Thalmann, Urs E. Studer*

Department of Urology, University of Bern, Bern, Switzerland

Abstract

**Background:** Prolonged postoperative pain and delayed intestinal transit are frequent problems following extended pelvic lymph-node dissection (PLND) and cystectomy.

**Objective:** To evaluate the impact of bilateral readaptation of the dorsolateral peritoneal layer on postoperative pain, gastrointestinal recovery, and complications following extended PLND and cystectomy.

**Design, setting, and participants:** Randomized, single-blinded, single-center study of 200 consecutive cystectomy patients.

**Intervention:** In group A ($n = 100$), lateral peritoneal flaps ventral to the external iliac vessels were bilaterally rotated over the iliac vessels down to the distal obturator fossa and medially fixed to the pararectal peritoneal layer following extended PLND and cystectomy. In group B ($n = 100$), the peritoneal layer was not readapted.

**Measurements:** Pain according to the visual analog scale (VAS), amount of peridural anesthetics needed, and gastrointestinal activity were assessed on postoperative days 1, 3, and 7. Complications occurring within 30 d following surgery were documented.

**Results and limitations:** Readaptation of the dorsolateral peritoneal layer resulted in a significant decrease in pain ($p < 0.01$) with concurrent significantly reduced need for peridural anesthetics ($p < 0.01$). Flatulence and first passage of stool as signs of intestinal transit were noted earlier in group A than in group B. Gastrostomy tube and peridural catheter could be removed 1 d earlier in group A than in group B (postoperative days 7 vs 8 and 6 vs 7, respectively). Group A (30%) had fewer complications than group B (56%; $p < 0.001$).

**Conclusions:** Readaptation of the dorsolateral peritoneal layer after extended PLND and cystectomy resulted in significantly less postoperative pain, earlier recovery of bowel function, and fewer complications in the early postoperative period.
1. Introduction

Prolonged postoperative pain, delayed intestinal transit, as well as gastrointestinal, pulmonary, and thromboembolic complications are common problems following extended pelvic lymph-node dissection (PLND) and cystectomy. They are related to surgery and not to diversion [1]. Early complications (<30 d after surgery) occur in 20–58% of patients following PLND and cystectomy [1–6]. Among the most frequent complications are gastrointestinal problems, which are reported to affect ≤29% of all cystectomy patients without clearly defining whether they comprise small bowel palsy, obstruction, ileus, or constipation.

One reason for this high incidence might be surgery-induced inflammatory reactions that arise between the small bowel and the deperitonealized pelvic wall. This and the ensuing adhesions might reduce bowel peristalsis, cause mechanical obstruction with pain, and, as a consequence, retard the patient’s mobilization with an increase in postoperative complications such as atelectasis, pneumonia, deep venous thrombosis, and pulmonary embolism. To overcome this problem, an increasing number of adhesion-reducing agents in the form of site-specific solutions, such as icodextrin and broad-coverage barriers, are becoming available [7–11]. There is, however, some controversy regarding their efficacy.

A more natural approach is to reperitonealize the abdominal cavity during surgery. Retropertioneal aortic replacement for aneurysm, for example, has been shown to significantly reduce postoperative ileus and the need for postoperative respiratory support, thus shortening the length of stay in the intensive care unit compared with the transabdominal approach [12].

In the present prospective randomized trial we evaluate the impact of bilateral reperitonealization of the dorsolateral pelvic walls with autologous peritoneal flaps on postoperative pain management, gastrointestinal recovery, and complications following extended PLND and cystectomy.

2. Methods

2.1. Patients

Between April 2006 and September 2009, 200 consecutive patients (median age: 67 yr; range: 30–86) scheduled for extended PLND and radical cystectomy due to urinary bladder malignancy were prospectively randomly assigned by a computer-based program into two groups of 100 patients each: one to undergo readaptation of the peritoneum, the other not. Exclusion criteria were bladder cancer higher than cT3 and previous PLND. The study was approved by the local ethics committee and all patients gave their informed consent.

2.2. Surgical technique

In group A, the lateral peritoneal layer was incised dorsomedially (Fig. 1a) and mobilized off the external iliac vessels on both sides to maintain large lateral peritoneal flaps (Fig. 1b). Following PLND, cystectomy, and urinary diversion, the peritoneal flaps ventrolateral to the external iliac vessels were rotated over the iliac vessels down to the distal obturator fossa and fixed with a mattress suture to the levator ani medial and dorsal to the obturator nerve. The medial border of the flap was then readapted and sutured to the rim of peritoneum along the rectum with interrupted 2-0 polyglycolic acid sutures at a distance of approximately 3 cm to prevent postoperative lymphoceles (Fig. 1c). A silicon drain without suction was placed between the vessels and the peritoneum on both sides (Fig. 1c).

In group B, the lateral parietal peritoneum was incised above the external iliac artery (Fig. 1d) without creating peritoneal flaps for readaptation of the dorsolateral peritoneal layer at the end of the operation (Fig. 1e–f). In these patients, two silicon wound drains without suction were placed: one close to the uretero-ileoanastomosis and one in the region of the urethro-neovesical anastomosis.

2.3. Patient management

Preoperative bowel preparation consisted of two high enemas. All patients had a gastrostomy tube placed that initially was left on drainage. It was removed once the patient passed stool and tolerated closure of the gastrostomy tube without nausea and vomiting for >24 h; however, for safety reasons, it was not removed earlier than postoperative day 5. To stimulate postoperative bowel function, subcutaneous injections of parasympathomimetic drugs (0.5 mg neostigmine methylsulfate up to six times per day) were administered starting on postoperative day 2 and continuing until bowel activity resumed. Antiemetics were only given on request. Oral diet was initiated with fluids on the day of surgery or on postoperative day 1 and then gradually advanced to solids as tolerated.
A low thoracic (Th9–10) epidural catheter was placed preoperatively and combined anesthesia (general and epidural) was given intraoperatively. Both groups were given epidural analgesia consisting of 1 mg/ml bupivacaine hydrochloride, 2 mcg/ml fentanyl citrate, and 2 mcg/ml adrenaline in NaCl 0.9% administered via a peridural catheter. Postoperatively, the initial infusion rate for the peridural anesthetics was 8 ml/h. This was increased or reduced in steps of 2 ml/h according to the pain score assessed by the numeric rating scale. Fluid administration during surgery was restricted. Perioperative antibiotic therapy consisted of garamycin and metronidazole for 2 d and amoxicillin/clavulanic acid until removal of all stents and catheters. Low-molecular-weight heparin (Fraxiparine) injected into the arm was started on the evening before surgery and maintained for at least 10 d.

The parameters assessed on postoperative days 1, 3, and 7 were pain score according to the visual analog scale (VAS), amount of peridural anesthetics needed, and recovery of bowel function as measured by the parameters nausea, vomiting, flatulence, and passage of stool. We also assessed the duration of peridural catheter and gastrostomy tube placement, time to mobilization (walking >10 m without assistance), length of hospitalization, and complications occurring within 30 d of surgery according to the Clavien-Dindo classification [13]. All parameters were assessed by a nurse blinded to the study. Independent physicians of the hospital's pain service and who did not assist in the operation were responsible for patients' pain management.

2.4. Statistical analysis

Statistical analysis was performed by the Institute of Social and Preventive Medicine of the University of Bern, Switzerland, with the Stata 10.0 program (StataCorp, College Station, TX, USA) using the Pearson chi-square test for dichotomous variables and the Wilcoxon rank-sum test for continuous variables. The sample size of 200 patients (n = 100 for each group) with a two-sided significance level of 5% (α = 0.05) and a power of 80% (β = 0.2) was based on the assumption that the complication rate is 10% in the group with and 23% in the group without reperitonealization.

3. Results

Preoperative patient characteristics were similar and the types of urinary diversions performed were evenly distributed. The median time of surgery did not differ between the two groups (Table 1). At least one of three senior staff members was involved in 97% of all surgeries in group A and in 99% in group B (p = 0.31). The pathologic features are listed in Table 1.

Closure of the dorsolateral peritoneal layer in group A resulted in a significant decrease in pain on postoperative days 1, 3, and 7, with a concurrent significantly reduced requirement for peridural anesthetics on days 1 and 7 (Fig. 2a–b). Peridural catheters were removed earlier in group A than in group B (postoperative day 6 vs 7; p = 0.03).

The difference in time to mobilization did not reach statistical significance (postoperative day 3 in group A vs postoperative day 4 in group B; p = 0.17).

Significantly fewer patients in group A with closure of the dorsolateral peritoneal layer had nausea on postoperative day 7 than patients in group B (29% vs 45%; p = 0.019)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group A with reperitonealization (n = 100)</th>
<th>Group B without reperitonealization (n = 100)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, yr (range)</td>
<td>68 (35–86)</td>
<td>65 (30–86)</td>
<td>0.165</td>
</tr>
<tr>
<td>Gender, No. (%)</td>
<td></td>
<td></td>
<td>0.282</td>
</tr>
<tr>
<td>Male</td>
<td>73 (73)</td>
<td>66 (66)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>27 (27)</td>
<td>34 (34)</td>
<td></td>
</tr>
<tr>
<td>BMI, median (range)</td>
<td>26.2 (19.0–40.9)</td>
<td>25.3 (17.7–40.3)</td>
<td>0.745</td>
</tr>
<tr>
<td>Diabetes, No. (%)</td>
<td>9 (9)</td>
<td>9 (9)</td>
<td>1.000</td>
</tr>
<tr>
<td>Chronic constipation, No. (%)</td>
<td>12 (12)</td>
<td>9 (9)</td>
<td>0.534</td>
</tr>
<tr>
<td>ASA score, No. (%)</td>
<td></td>
<td></td>
<td>0.401</td>
</tr>
<tr>
<td>I</td>
<td>11 (11)</td>
<td>6 (6)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>50 (50)</td>
<td>60 (60)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>37 (37)</td>
<td>33 (33)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>2 (2)</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>Prior radiotherapy, pelvis, No. (%)</td>
<td>6 (6)</td>
<td>3 (3)</td>
<td>0.306</td>
</tr>
<tr>
<td>Neoadjuvant chemotherapy, No. (%)</td>
<td>16 (16)</td>
<td>19 (19)</td>
<td>0.577</td>
</tr>
<tr>
<td>Prior abdominal surgery, No. (%)</td>
<td>34 (34)</td>
<td>22 (22)</td>
<td>0.059</td>
</tr>
<tr>
<td>Urinary diversion, No. (%)</td>
<td></td>
<td></td>
<td>0.273</td>
</tr>
<tr>
<td>Ileal conduit</td>
<td>35 (35)</td>
<td>29 (29)</td>
<td></td>
</tr>
<tr>
<td>Orthotopic neobladder</td>
<td>63 (63)</td>
<td>65 (65)</td>
<td></td>
</tr>
<tr>
<td>Catheterizable pouch</td>
<td>2 (2)</td>
<td>6 (6)</td>
<td></td>
</tr>
<tr>
<td>Median time for surgery, min (range)</td>
<td>390 (195–490)</td>
<td>390 (225–480)</td>
<td>0.762</td>
</tr>
<tr>
<td>Pathologic tumour stage, No. (%)</td>
<td></td>
<td></td>
<td>0.556</td>
</tr>
<tr>
<td>pTis/pTa</td>
<td>7 (7)</td>
<td>7 (7)</td>
<td></td>
</tr>
<tr>
<td>pT1</td>
<td>13 (13)</td>
<td>21 (21)</td>
<td></td>
</tr>
<tr>
<td>pT2</td>
<td>29 (29)</td>
<td>30 (30)</td>
<td></td>
</tr>
<tr>
<td>pT3</td>
<td>41 (41)</td>
<td>32 (32)</td>
<td></td>
</tr>
<tr>
<td>pT4</td>
<td>10 (10)</td>
<td>10 (10)</td>
<td></td>
</tr>
<tr>
<td>Pathologic lymph node status, No. (%)</td>
<td></td>
<td></td>
<td>0.428</td>
</tr>
<tr>
<td>pN0</td>
<td>75 (75)</td>
<td>70 (70)</td>
<td></td>
</tr>
<tr>
<td>pN+</td>
<td>25 (25)</td>
<td>30 (30)</td>
<td></td>
</tr>
</tbody>
</table>

BMI = body mass index; ASA = American Society of Anesthesiologists.
The antiemetic metoclopramide was given to 12 patients in group A and 13 patients in group B ($p = 0.83$). The number of vomiting episodes were comparable between the two groups. Flatulence was noted earlier in group A and reached statistical significance ($p = 0.016$) on postoperative day 3 (Fig. 2d). In group A, 95% of patients passed stool by day 7 versus 84% of group B ($p = 0.011$) (Fig. 2e). Median time to gastrostomy tube removal was 7 d in group A and 8 d in group B ($p = 0.093$). The median duration of hospitalization did not differ between the two groups (16.5 vs 17 d; $p = 0.848$).

There were significantly fewer complications in group A than in group B (30% vs 56%; $p < 0.001$) (Fig. 2f). Most of the complications were minor (grade 1 or grade 2). A detailed summary of complication types and distribution between the two groups is given in Table 2.

### 4. Discussion

To our knowledge, this is the first study assessing the impact of reperitonealization on early postoperative recovery and complications following PLND and cystectomy. Readaptation of the dorsolateral peritoneal layers led to improved gastrointestinal transit: Flatulence and first passage of stool occurred earlier and fewer patients suffered nausea. In the early postoperative period, the patients without readaptation of the dorsolateral peritoneal layers (group B) had significantly more pain according to the VAS.
needed larger amounts of peridural anesthetics, and the peridural catheter remained longer in situ. Significantly more complications occurred in this group.

In the early postoperative period, intra-abdominal adhesions due to events such as inflammatory reactions or small serosa lesions frequently occur in patients following PLND and cystectomy. These adhesions may cause small bowel palsy, paralytic ileus, bloating, or constipation, and represent a significant, though temporary, postoperative problem. Extensive adhesions between small bowel loops and the abdominal and pelvic walls or the iliac vessels are often found in patients who have to undergo reoperation following PLND and cystectomy. Small bowel adhesions may cause mechanical obstruction [14]. For PLND and cystectomy, urologic surgery textbooks advocate incising the peritoneum into the deep pelvis on each side of the lateral umbilical ligaments and above the external iliac vessels. This makes a reperitonealization that covers the iliac vessels and the obturator fossa hardly possible. Therefore, we incised the lateral parietal peritoneum more dorsally to the external iliac vessels and peeled it off these vessels in a ventral direction so as to create bilateral autologous peritoneal flaps (Fig. 1a–b). After PLND, cystectomy, and urinary diversion, the continuity of the dorsolateral parietal peritoneum is restored by rotating the peritoneal flaps over the external iliac vessels down to the distal obturator fossa, where it is fixed with separate stitches. This quickly performed procedure did not expose patients to an additional risk and improved gastrointestinal transit, even though more patients in the reperitonealization group had a history of abdominal surgery. Readaptation of
the dorsolateral peritoneal layers therefore appears to be a inexpensive and efficacious way to accelerate postoperative recovery with autologous peritoneum.

The significant difference in pain is an interesting finding although the reasons are not fully understood. As others have pointed out, adhesions may cause pain [15–17], probably due to overexpressed sensory nerve fibers in the adhesions. Still, nerve fiber growth is not fast enough to cause more pain in the early postoperative period. Another reason may be rubbing of the visceral peritoneum against the uncovered, rough surface of the dorsolateral pelvic walls. Whatever the case, the causal association between abdominal or pelvic pain and postoperative adhesions remains undetermined.

A higher incidence of postoperative lymphoceles after reperitonealization was one of our major concerns at the beginning of this trial since adaptation of the dorsolateral parietal peritoneum over the iliac vessels might block lymph drainage into the peritoneal cavity where the lymph fluid is reabsorbed. Surprisingly, the incidence of symptomatic lymphoceles was equal in the two groups (9%). This finding might be attributed to the suture technique: The single, interrupted sutures were not too close to enable lymph drainage, but close enough to prevent internal hernias. Still, 9% appears to be a high incidence. We attribute this to the fact that we regularly looked for lymphoceles by ultrasound and did not hesitate to place (under local anesthesia) an ultrasound-guided 10F nephrostomy tube or a 12-F cystostomy tube into any detectable collection in order not to retard the postoperative evolution and hospital discharge.

Complications were assessed applying the Clavien-Dindo classification system [13], a validated tool that has been adopted by several urology centers [2,18,19]. Our overall 43% complication rate is in line with the results from other major centers [1–6,20–22]. Most of our complications, however, were minor (grade 1 or 2). Especially for grade 1 complications (comprising any deviation from normal course), it is often a matter of discretion if they are counted as a complication or not. Absence of bowel peristalsis on postoperative day 5, for example, was counted as a complication in our cohort, whereas others may regard this as being in line with a normal postoperative course. Fewer total complications were observed in our patients undergoing readaptation of the dorsolateral peritoneal layers (30% vs 56%). Although the difference is significant, we cannot exclude other factors which may have contributed to this result. Among these are less postoperative pain or earlier removal of catheters (eg, peridural catheter, gastrostomy tube), each leading to earlier mobilization and thus to a reduction in immobilization-associated complications such as deep venous thrombosis, pulmonary embolism, atelectasis, and pneumonia. The difference in the rate of complications did not affect the length of hospital stay, mainly for two reasons: first, most complications were minor complications with no influence on postoperative recovery. Second, at our institution, ileal bladder-substitute patients are instructed how to self-manage the urostoma before they leave the hospital. This takes time irrespective of the postoperative course. In return, our rehospitalization rate in the 30 d after discharge is very low (1.5%).

Lower complication rates and faster recovery have been reported for extraperitoneal cystectomy, albeit not based on a randomized trial [23]. As there may be concern about the radicalness of surgery in extraperitoneal cystectomy, we prefer the resection of the peritoneum covering and adjunct to the bladder followed by the reperitonealization with rotated peritoneal flaps. The abdominal cavity closure is not complete, but it is, as our results suggest, sufficient to significantly improve postoperative recovery and lower the complication rate.

A potential limitation of this randomized trial is that it tested only one method of retroperitonealization; other methods may be possible. Another point of criticism might be that complications treated outside our institution are underreported. However, our patients’ regular, short-term, postoperative visits on an outpatient basis reduced the probability that any complications were missed.

5. Conclusions

Readaptation of the dorsolateral peritoneal layers following extended PLND and cystectomy improves postoperative recovery of bowel function and leads to less postoperative pain and fewer complications. The procedure is easy, inexpensive, safe, and quickly performed. We therefore recommend reperitonealization following extended PLND and cystectomy.

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: Roth, Studer, Burkhard.

Acquisition of data: Roth, Birkhaeuser, Zehnder.

Analysis and interpretation of data: Roth, Studer.

Drafting of the manuscript: Roth.

Critical revision of the manuscript for important intellectual content: Studer, Thalmann, Birkhaeuser, Zehnder.

Statistical analysis: None.

Obtaining funding: None.

Administrative, technical, or material support: None.

Supervision: Studer, Roth.

Other (specify): None.

Financial disclosures: I certify that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: None.

Consultancies, honoraria, stock ownership or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending).

References


