Influence of Epidural Mixture and Surgery on Bladder Function after Open Renal Surgery
A Randomized Clinical Trial

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ABSTRACT

Background: In a previous observational study, thoracic epidural analgesia (TEA) after open renal surgery resulted in clinically relevant postvoid residuals (PVRs). This study aimed to investigate the individual contribution of epidurally administrated drugs and surgery in bladder dysfunction.

Methods: In this single-center, parallel-group, randomized (computer-generated list), double-blind superiority trial, 40 patients undergoing open renal surgery were equally allocated to receive epidural bupivacaine (0.125%) alone or with fentanyl (2 μg/ml). Patients underwent urodynamic investigations before TEA and during TEA preoperatively and postoperatively. Primary outcome was the difference (Δ) in PVR between before TEA and postoperatively during TEA. Secondary outcomes were changes in detrusor pressure at maximum flow rate, bladder compliance, and ΔPVR between different time points.

Results: Median ΔPVR (ml) from baseline to postoperatively was 180 (range, −85 to 645; P = 0.001) in the bupivacaine group and 235 (range, 0–580; P value less than 0.001) in the bupivacaine/fentanyl group, with no difference between groups (95% confidence interval, −167 to 103; P = 0.634). Detrusor pressure at maximum flow rate (cm H₂O) from baseline was more pronounced in the bupivacaine/fentanyl than that in the bupivacaine group preoperatively (−10; range, −64 to −2; P value less than 0.001 vs. −3; range, −35 to 13; P = 0.397) and postoperatively (−18; range, −64 to 0; P value less than 0.001 vs. −12; range, −34 to 22; P = 0.006) (P = 0.135). Surgery did not affect PVRs, but a decreased bladder compliance was observed in both groups. No adverse events occurred.

Conclusions: Thoracic epidurally administrated bupivacaine resulted in clinically relevant PVRs based on impaired detrusor function. The addition of fentanyl enhanced this effect without generating greater PVRs. After surgery, the voiding phase was not further impaired; however, bladder compliance was decreased.

What We Already Know about This Topic

• Thoracic epidural analgesia after open renal surgery has previously been shown to result in clinically important postvoid residual volumes, but whether this is due to the local anesthetic or adjunctive opioid is unclear.

What This Article Tells Us That Is New

• In a study of 40 patients undergoing open renal surgery randomized to receive thoracic epidural analgesia with bupivacaine alone or with fentanyl, postvoid residual volumes were unaffected by addition of fentanyl, suggesting an effect of epidural bupivacaine per se.

Urine retention is one of the most common postoperative complications with a reported incidence of 5–70%.1 It is linked to several factors including increased intravenous fluid administration, postoperative pain, use of opioids, and neuraxial anesthesia.2 The treatment of choice is bladder catheterization, which is associated with relevant morbidity such as patient discomfort, urethral trauma, urethral stricture, and urinary tract infections. The risk of urinary tract infection with a single catheterization is 1–2% and can rise by 5–10% for every additional day with an indwelling catheter.2 It is the most common nosocomial infection in the United States, accounting for more than 1 million cases each year and 900,000 additional hospital days per year. Urinary tract infection is directly responsible for 13% of deaths related to nosocomial infections3 and is associated with high financial implications.4
Thoracic epidural analgesia (TEA) has been shown to provide effective analgesia and to facilitate postoperative rehabilitation. It has been common practice to continue urinary drainage in patients receiving continuous postoperative epidural analgesia.

In our previous studies, we observed, against our expectations, that during TEA with bupivacaine, fentanyl, and epinephrine, the detrusor was significantly inhibited; this resulted in clinically relevant postvoid residuals (PVRs), which required monitoring or catheterization. Because the studies adopted a before and after design with no control group, we could not definitively identify the mechanisms responsible for lower urinary tract dysfunction.

The objective of this study was to investigate the role of epidurally administered drugs and surgery in bladder dysfunction. The primary hypothesis was that the addition of fentanyl to bupivacaine enhances lower urinary tract dysfunction. The secondary hypothesis was to delineate whether open renal surgery affects bladder function.

Materials and Methods

Trial Design and Patients
This single-center, randomized, double-blind, parallel-groups study was approved by the local ethics committee of the University Hospital of Bern (KEK Bern, Switzerland) and registered at ClinicalTrials.gov (NCT01220362). Patients planned for open renal surgery were screened for inclusion at the urological clinic of the University Hospital of Bern. All recruited patients completed the validated International Prostate Symptom Score questionnaire. Only patients with no preexisting lower urinary tract symptoms (International Prostate Symptom Score less than 7) and a PVR value less than 100 ml (assessed by ultrasound) were included after providing written informed consent. Exclusion criteria were any contraindication to TEA and systemic opioid administration postoperatively.

Forty patients were equally randomly allocated to either TEA with bupivacaine 0.125% or bupivacaine 0.125% plus fentanyl 2 µg/ml by a computer-generated randomization list without blocking, following the recommendation of the Consolidated Standards of Reporting Trials statements (fig. 1). The allocation sequence was prepared by an independent operator not involved in the study, and the allocation assignment was concealed in opaque sealed envelopes that were sequentially numbered. Patients were allocated to the treatment group by assigning them the sequentially numbered envelope with the lowest number before receiving the thoracic epidural catheter. Patients and investigators of bladder function were blinded to the epidural solution administrated: The contents of the epidural mixture were not distinguishable as the vials were placed in a sealed opaque bag before the patient and investigator entered the urodynamic room by an anesthesiologist not involved in the study.

Time Course and Intervention
After recruitment, the first urodynamic investigation was performed before TEA. Urodynamic investigations were performed according to good urodynamic practice. After placement of a 6F transurethral dual channel catheter and a 14F rectal balloon catheter (Gaeltec, Dunvegan, Scotland), the bladder was filled at a rate of 25–50 ml/min with Ringer lactate solution at room temperature. Parameters of both the storage phase (maximum cystometric capacity, bladder compliance) and voiding phase (detrusor pressure at maximum flow rate, Pdet Qmax), maximum flow rate (Qmax), and PVR were recorded. A TRITON multichannel urodynamic system was used for all measurements (Laborie Medical Technologies Corp., Toronto, Ontario, Canada). All methods, definitions, and units are in accordance with the standards recommended by the International Continence Society.

After removal of the epidural catheter on the fifth postoperative day, the PVR was documented noninvasively by ultrasound after the first micturition.

All patients received a thoracic epidural catheter placed at the interspace T8 to T9 the day before surgery. The insertion site was determined using the classic landmark method, whereby the spinal process of T7 was identified at the line intersecting the inferior tip of the scapulae in the sitting position. An 18-gauge epidural needle was inserted by a paramedian approach, and the epidural space was identified with the loss-of-resistance technique. A test dose of 1.5 ml lidocaine (20 mg/ml) with 0.005 mg/ml epinephrine was given to rule out subarachnoidal or intravascular placement. Segmental blockade above T6 and below T10 not exceeding T12 bilaterally was achieved by injecting 2-ml increments for 10 min, using the solutions according to the randomization: 1.25 mg/ml bupivacaine (“bupivacaine group”) (Bupivacain 0.125% Bioren; Sintetica-Bioren, Couvet, Switzerland) or 1.25 mg/ml bupivacaine plus 2 µg/ml fentanyl (“bupivacaine/fentanyl group”) (Bupivacain–Fentanyl Sintetica; Sintetica-Bioren). The level of sensory blockade was assessed by hyposensitivity to cold. A cold gel bag with a surface of 4 cm² was applied for 1 s to each dermatome (cold gel bag, Nexcare reusable cold pack; 3M, St Paul, MN). The second urodynamic investigation during TEA was performed 20 min after assessment of the adequate segmental blockade (fig. 1). After this assessment, the epidural catheter was left in place and no drugs were infused.

TEA was then reactivated 20 min before skin incision with 2.5 mg/ml bupivacaine at a rate of 6–10 ml/h in both groups. Similar to our previous study, no opioids were administrated epidurally during surgery. General anesthesia was induced with propofol, fentanyl, and atracurium and maintained with isoflurane. A transurethral catheter was inserted after induction and left in place until the next urodynamic investigation. At the end of surgery, continuous epidural analgesia was maintained with the epidural mixtures according to the randomized groups, using a CADD Legacy ambulatory infusion pump (model 6300; Deltec Inc., St Paul, MN).
The initial infusion rate was 8 ml/h, with additional bolus volumes of 5 ml (lockout time, 1 h). The infusion rate was then adapted if necessary based on assessments made every 4 h to maintain a pain intensity lower than 3 at rest and lower than 5 during mobilization on the numeric rating scale, where 0 = no pain and 10 = worst pain imaginable. The maximum infusion rate was 15 ml/h. Paracetamol (1,000 mg) every 6 h was administered as a supplement for postoperative analgesia. The systemic administration of opioids was only used as a rescue requirement if the numeric rating scale was higher than 5 after optimization of the TEA.

The third urodynamic investigation was performed on the second postoperative day at around noon. Segmental blockade was assessed at 8:00 AM, and if necessary, the epidural mixture rate was optimized to achieve a segmental blockade above T6 and below T10, not exceeding T12 bilaterally (fig. 1). Potential risk factors for postoperative urinary retention (postoperative rescue opioid requirement, postoperative nausea and vomiting, and sedation) were also documented.

After removal of the epidural catheter on the fifth postoperative day, PVR was documented noninvasively by ultrasound after the first micturition.
Fentanyl Assay
Four milliliters of blood was collected in a heparinized tube immediately before the third urodynamic investigation. The collected blood was immediately placed on ice and centrifuged at 4°C (2000g, 30 min). The supernatant plasma was then transferred to silanized glass vials with a screw cap and stored at −20°C until analysis. The plasma fentanyl concentrations were determined by the Department of Clinical Research of the University Hospital Bern. The concentrations were measured using gas chromatography with mass spectrometry (Agilent 6890; Hewlett-Packard, Palo Alto, CA). The minimum detectable plasma fentanyl concentration was 0.05 ng/ml. All probes were analyzed at the same time.

Endpoints
The primary endpoint was as follows:

− Within-patient difference (Δ) in PVR (Δ = value during TEA postoperatively − value before TEA) between the two groups.

The secondary endpoints were as follows:

− Within-patient difference in maximum cystometric capacity, bladder compliance, \( P_{\text{det}} Q_{\text{max}} \), \( Q_{\text{max}} \) and PVR between two time points:

1) during TEA preoperatively versus before TEA,
2) during TEA postoperatively versus before TEA, and
3) during TEA postoperatively versus preoperatively.

− The occurrence of urinary tract infections requiring antibiotic treatment and pain in the urinary tract requiring analgesic treatment as a consequence of urodynamic investigations.

Statistical Analysis
This randomized superiority study was designed to have 80% power to detect a between-group difference in within-patient PVR difference (Δ) of 230 ml during TEA postoperatively versus before TEA using a two-sided \( t \) test at a significance level of 5%, assuming an SD of 110 ml (PASS 2005; NCSS, Kaysville, UT). Such a difference is considered clinically relevant. This resulted in a sample size of 40 patients, that is, 20 patients in the bupivacaine group and 20 patients in the bupivacaine/fentanyl group. In general, for quantitative endpoints, the two groups were compared using Wilcoxon rank sum test, accompanied with nonparametric 95% confidence interval (CI). Within each group, the within-patient preoperative–postoperative differences were analyzed using the Wilcoxon signed rank test. Categorical endpoints were analyzed using the Fisher exact test. To control overall type I error for multiple testing of each secondary endpoint, the Bonferroni approach was applied to each family of within-group or between-group tests of within-patient differences from three pairs of time points. A two-sided \( P \) value less than 0.05 was considered statistically significant. The statistical software used was the Statistical Package for the Social Sciences Version 19.0 (SPSS Inc., Chicago, IL) and R version 2.12.1 (The R Foundation for Statistical Computing, Vienna, Austria).

Results
Between September 2010 and November 2011, a total of 48 patients were assessed for eligibility and 40 patients underwent randomization (fig. 1). Baseline characteristics were similar between the two groups, with the exception of a more cranial spread of the segmental blockade in the bupivacaine group (table 1). No patient dropped out. No systemic opioids and no sedatives were administrated postoperatively, and no postoperative nausea and vomiting were documented. No motor blockade related to TEA was present (Bromage motor block score of zero in all patients).

Change in Urodynamic Results during TEA Postoperatively versus before TEA
Median ΔPVR during TEA postoperatively versus before TEA was 180 ml in the bupivacaine group (range, −85 to 645; \( P = 0.001 \)) and 235 ml in the bupivacaine/fentanyl group (range, 0–580; \( P < 0.001 \)) (table 2; fig. 2). No statistically significant difference in ΔPVR between the two groups was observed (95% CI, −167 to 103; \( P = 0.634 \)). In seven patients (35%) in the bupivacaine group and in five patients (25%) in the bupivacaine/fentanyl group, the PVR remained less than 100 ml during TEA postoperatively (\( P = 0.731 \)).

The median Δ\( P_{\text{det}} Q_{\text{max}} \) was −12 cm H\(_2\)O (range, −34 to 22; \( P = 0.006 \)) in the bupivacaine group and −18 cm H\(_2\)O (range, −64 to 0; \( P < 0.001 \)) in the bupivacaine/fentanyl group and was more pronounced in the bupivacaine/fentanyl group (95% CI, 0–22; \( P = 0.135 \)). The median Δ\( Q_{\text{max}} \) was −8.5 ml/s (range, −23 to 3; \( P = 0.005 \)) in the bupivacaine and −9.5 ml (range, −31 to 7; \( P = 0.002 \)) in the bupivacaine/fentanyl group. Four patients in the bupivacaine group (20%) and eight patients in the bupivacaine/fentanyl group (40%) had a \( Q_{\text{max}} \) of 0 ml/s (\( P = 0.301 \)) during TEA postoperatively and were unable to void. The median Abladder compliance was −48 ml/cm H\(_2\)O (range, −473 to 45; \( P < 0.001 \)) in the bupivacaine group and −44 ml/cm H\(_2\)O (range, −108 to 34; \( P = 0.011 \)) in the bupivacaine/fentanyl group.

The median plasma fentanyl concentration on postoperative day 2 was 0.31 ng/ml (range, 0.09-1.45) in the bupivacaine/fentanyl group.

Change in Urodynamic Results during TEA Preoperatively versus before TEA
The median ΔPVR was 190 ml (range, −60 to 695; \( P < 0.001 \)) in the bupivacaine group and 385 ml (range, 15–840; \( P < 0.001 \)) in the bupivacaine/fentanyl group (table 3; fig. 2). The median Δ\( P_{\text{det}} Q_{\text{max}} \) was −3 cm H\(_2\)O (range, −35 to 13; \( P = 0.397 \)) in the bupivacaine group and −10 cm H\(_2\)O (range, −64 to −2; \( P < 0.001 \)) in the bupivacaine/fentanyl group.
Bladder Function during Thoracic Epidural Analgesia

Change in Urodynamic Results during TEA Postoperatively versus Preoperatively

No relevant changes were observed in $\Delta P_{\text{det}} Q_{\text{max}}$, and $\Delta P_{\text{det}} Q_{\text{max}}$ during TEA postoperatively versus preoperatively (table 4; fig. 2) in both groups. Maximum cystometric capacity and bladder compliance were statistically significant in the bupivacaine group, $-105$ ml (range, $-555$ to $50$; $P = 0.001$) and $-25$ ml/cm H$_2$O (range, $-194$ to $16$; $P = 0.002$), and in the bupivacaine/fentanyl group, $-205$ ml (range, $-425$ to $125$; $P = 0.004$) and $-27$ ml/cm H$_2$O (range, $-250$ to $37$; $P = 0.022$). There was no difference between the groups.

The median PVR after removal of TEA on postoperative day 5 was $0$ ml (range, $0$–$70$) in the bupivacaine group and $2.5$ ml (0–140) in the bupivacaine/fentanyl group ($P = 0.978$).

No adverse events (urinary tract infections and pain in the urinary tract requiring analgesic treatment) related to the urodynamic investigations occurred.

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Bupivacaine Group (n = 20)</th>
<th>Bupivacaine/Fentanyl Group (n = 20)</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>61 (43–85)</td>
<td>63 (42–75)</td>
<td>0.989</td>
</tr>
<tr>
<td>Sex (women/men)</td>
<td>7/13</td>
<td>8/12</td>
<td>1</td>
</tr>
<tr>
<td>ASA Classification (II/III)</td>
<td>11/9</td>
<td>8/12</td>
<td>0.341</td>
</tr>
<tr>
<td>IPSS</td>
<td>3 (0–6)</td>
<td>2 (0–7)</td>
<td>0.640</td>
</tr>
<tr>
<td>Bolus of epidural mixture preoperatively, ml</td>
<td>5.5 (3–8)</td>
<td>5.0 (3–8)</td>
<td>0.953</td>
</tr>
<tr>
<td>Epidural mixture rate postoperatively, ml/h</td>
<td>8.0 (4–12)</td>
<td>8.0 (4–12)</td>
<td>0.171</td>
</tr>
<tr>
<td>NRS at rest</td>
<td>0 (0–2)</td>
<td>0 (0–1)</td>
<td>0.938</td>
</tr>
<tr>
<td>NRS during mobilization</td>
<td>2 (0–5)</td>
<td>2 (0–4)</td>
<td>0.582</td>
</tr>
<tr>
<td>Segmental blockade before surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper thoracic dermatome</td>
<td>4 (4–6)</td>
<td>4 (4–6)</td>
<td>0.633</td>
</tr>
<tr>
<td>Lower thoracic dermatome</td>
<td>11 (10–12)</td>
<td>11 (10–12)</td>
<td>0.657</td>
</tr>
<tr>
<td>Segmental blockade after surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper thoracic dermatome</td>
<td>4 (3–5)</td>
<td>5 (4–6)</td>
<td>0.047*</td>
</tr>
<tr>
<td>Lower thoracic dermatome</td>
<td>12 (11–12)</td>
<td>11 (10–12)</td>
<td>0.062</td>
</tr>
<tr>
<td>Intraoperative dose of intravenous fentanyl, mg</td>
<td>0.4 (0.2–0.7)</td>
<td>0.4 (0.15–0.60)</td>
<td>0.891</td>
</tr>
</tbody>
</table>

Data are presented as counts or median values (range).
* Two-sided $P < 0.05$ as statistically significant.

ASA = American Society of Anesthesiologists; IPSS = International Prostate Symptom Score; NRS = numeric rating scale for pain (0 = no pain, 10 = worst pain imaginable).

Table 2. Within-patient Difference ($\Delta$) between Two Time Points: TEA Postoperatively versus before TEA

<table>
<thead>
<tr>
<th></th>
<th>Bupivacaine Group (n = 20)</th>
<th>Bupivacaine/Fentanyl Group (n = 20)</th>
<th>Between-Group Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (Range), $P$†</td>
<td>Median (Range), $P$†</td>
<td>95% CI, $P$‡</td>
</tr>
<tr>
<td>$\Delta P_{\text{det}} Q_{\text{max}}$, cm H$_2$O</td>
<td>$-12$ (−34 to 22), 0.006*</td>
<td>$-18$ (−64 to 0), &lt;0.001*</td>
<td>$-167$ to $103$, 0.634</td>
</tr>
<tr>
<td>$\Delta Q_{\text{max}}$, ml/s</td>
<td>$-8.5$ (−23 to 3), 0.005*</td>
<td>$-9.5$ (−31 to 7), &lt;0.002*</td>
<td>$-4$ to 9, 1.000</td>
</tr>
<tr>
<td>$\Delta$Compliance, ml/cm H$_2$O</td>
<td>$-48$ (−473 to 45), &lt;0.001*</td>
<td>$-44$ (−108 to 34), 0.011*</td>
<td>$-60$ to 8, 0.596</td>
</tr>
<tr>
<td>$\Delta$Maximum cystometric capacity, ml</td>
<td>$-75$ (−420 to 270), 0.391</td>
<td>$-65$ (−285 to 115), 0.079</td>
<td>$-115$ to 120, 1.000</td>
</tr>
</tbody>
</table>

* Two-sided $P < 0.05$ as statistically significant. † Within-group $P$ value derived from the Wilcoxon signed rank test for within-patient preoperative–postoperative difference of each endpoint, with Bonferroni adjustment. ‡ Between-group $P$ value from the Wilcoxon rank sum test for within-patient preoperative–postoperative difference, with Bonferroni adjustment. 95% CI was constructed accordingly, but without Bonferroni adjustment.

CI = confidence interval; $P_{\text{det}} Q_{\text{max}}$ = detrusor pressure at maximum flow rate; PVR = postvoid residual; $Q_{\text{max}}$ = maximum flow rate; TEA = thoracic epidural analgesia.
To our knowledge, this is the first time that the effect of different epidural mixtures on lower urinary tract function preoperatively and postoperatively has been assessed in a randomized double-blind study. Segmental blockade from T4 to T12 was associated with a relevant impairment in voiding function with clinically relevant PVRs. This was due to detrusor underactivity during TEA in both groups, which was observed both preoperatively and postoperatively. The addition of fentanyl led to a more pronounced impairment of detrusor activity during TEA preoperatively, which resulted in a greater increase in PVR. After lumbotomy for renal surgery, bladder compliance and maximum cystometric capacity were reduced, but detrusor function and PVRs were not affected, excluding surgery as a cause of voiding dysfunction.

The median ΔPVR of 200 ml or more, which we observed in the bupivacaine/fentanyl group during TEA preoperatively and postoperatively, represents a clinically relevant impairment in voiding function, which is associated with an increased risk of complications. One factor is the associated higher risk of urinary tract infections. Truzzi et al. found that a PVR higher than 180 ml was associated with a higher risk of bacteriuria. Another possibly even more serious potential problem is (unrecognized) acute bladder retention, which may initiate hypoxia-induced damage to the detrusor with a resulting increase in extracellular matrix deposits in the long term. This in turn leads to a decreased detrusor contractility and significant impairment of bladder function. It is important to acknowledge the risk of retention in this setting as 12 patients (30%; 4 patients in the bupivacaine and 8 in the bupivacaine/fentanyl group) in our study could not void at all postoperatively, which represents an absolute indication for catheterization.

As we did not find a significant difference between groups during TEA postoperatively, it seems unlikely that a systemic effect of fentanyl is involved. In addition, the plasma fentanyl concentration measured on postoperative day 2 was lower than the mean reported minimum effective analgesic concentration (0.63 ng/ml) for intravenous infusion in patients undergoing abdominal surgery and corresponded to the plasma concentration observed in the infusion group in the study by Ginosar et al. Alternatively, a possible wider distribution and lumbar spread of bupivacaine with preferential blockade of the small myelinated fibers could have resulted in a selective autonomic involvement. The caudal distribution of sympathetic blockade is known to exceed the sensory blockade 20 min after a bolus of bupivacaine 0.25%, which may be similar to what we observed after induction of TEA before surgery.

Interestingly, intact bladder sensory function was present during TEA at all times: We did observe a transient significant increase in bladder capacity during TEA before surgery.

Discussion

To our knowledge, this is the first time that the effect of different epidural mixtures on lower urinary tract function preoperatively and postoperatively has been assessed in a randomized double-blind study. Segmental blockade from T4 to T12 was associated with a relevant impairment in voiding function with clinically relevant PVRs. This was due to detrusor underactivity during TEA in both groups, which was observed both preoperatively and postoperatively. The addition of fentanyl led to a more pronounced impairment of detrusor activity during TEA preoperatively, which resulted in a greater increase in PVR. After lumbotomy for renal surgery, bladder compliance and maximum cystometric capacity were reduced, but detrusor function and PVRs were not affected, excluding surgery as a cause of voiding dysfunction.

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Interestingly, intact bladder sensory function was present during TEA at all times: We did observe a transient significant increase in bladder capacity during TEA before surgery.
surgery, which returned to normal values postoperatively. This implies an intact afferent sacral innervation. The slight increase in bladder volume observed immediately during TEA preoperatively, however, combined with the more impaired detrusor contractility in the bupivacaine/fentanyl group, could explain the resulting higher PVR in this group at that time point.

Bladder compliance was reduced in both groups after surgery. This result is in accordance with our preceding publication, where a different epidural mixture was used (0.1% bupivacaine, 2 µg/ml fentanyl, and 2 µg/ml epinephrine). However, the decrease in bladder compliance in both groups did not fulfill the criteria for poor compliance (less than 10 ml/cm H₂O) according to the literature. The normal bladder is extremely compliant, creating little to no pressure during filling. Hypothetically, this could be caused by retroperitoneal surgery inducing a retroperitoneal irritation or modulatory dysreflexia, leading to higher detrusor tone during the storage phase. Alternatively, the longer duration of TEA or the ongoing drainage of the bladder through an indwelling catheter could be postulated to affect the storage phase.

Early catheter removal after surgery in an attempt to avoid or minimize the rate of urinary tract infections and urethral trauma has become a major focus of interest. However, proper assessment and monitoring of PVRs in patients with impaired lower urinary tract function during TEA as observed in our patient population after open renal surgery is mandatory to avoid the potential complications of significant PVRs and the risk of long-term debilitating morbidity, such as loss of bladder function after acute urinary retention.

We are aware of certain limitations of our study: silent voiding dysfunction may be unmasked during TEA or after surgery, and our study was not placebo controlled; however, placebo TEA for postoperative analgesia would give rise to ethical concerns. Another limitation is the lack of control with systemic fentanyl administration.

### Table 3. Within-patient Difference (Δ) between Two Time Points: During TEA Preoperatively versus before TEA

<table>
<thead>
<tr>
<th></th>
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<th>Bupivacaine/Fentanyl Group (n = 20)</th>
<th>Between-Group Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔPVR, ml</td>
<td>Median (Range), P†</td>
<td>Median (Range), P†</td>
<td>95% CI, P‡</td>
</tr>
<tr>
<td></td>
<td>190 (−60 to 695), &lt;0.001*</td>
<td>385 (15 to 840), &lt;0.001*</td>
<td>(−295 to −5), 0.143</td>
</tr>
<tr>
<td>ΔPdetOmax H₂O, cm</td>
<td>−3 (−35 to 13), 0.397</td>
<td>−10 (−64 to −2), &lt;0.001*</td>
<td>(3 to 20), 0.045*</td>
</tr>
<tr>
<td>Qmax, ml/s</td>
<td>−3 (−19 to 12), 0.083</td>
<td>−8.5 (−29 to 3), 0.002*</td>
<td>(−1 to 11), 0.364</td>
</tr>
<tr>
<td>ΔCompliance, ml/cm</td>
<td>−17.5 (−460 to 100), 0.436</td>
<td>10 (−63 to 273), 1.000</td>
<td>(−67 to 2), 0.230</td>
</tr>
<tr>
<td>H₂O</td>
<td>Maximum cystometric</td>
<td>75 (−115 to 330), 0.040*</td>
<td>(−80 to 90), 1.000</td>
</tr>
<tr>
<td>capacity, ml</td>
<td>Median (Range)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Two-sided P < 0.05 as statistically significant. † Within-group P value derived from the Wilcoxon signed rank test for within-patient preoperative–postoperative difference of each endpoint, with Bonferroni adjustment for this test. ‡ Between-group P value from the Wilcoxon rank sum test for within-patient preoperative–postoperative difference, with Bonferroni adjustment. The 95% CI was constructed accordingly, but without Bonferroni adjustment.

CI = confidence interval; PdetOmax = detrusor pressure at maximum flow rate; PVR = postvoid residual; Qmax = maximum flow rate; TEA = thoracic epidural analgesia.

### Table 4. Within-patient Difference (Δ) between Two Time Points: During TEA Postoperatively versus Preoperatively

<table>
<thead>
<tr>
<th></th>
<th>Bupivacaine Group (n = 20)</th>
<th>Bupivacaine/Fentanyl Group (n = 20)</th>
<th>Between-Group Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔPVR, ml</td>
<td>Median (Range), P†</td>
<td>Median (Range), P†</td>
<td>95% CI, P‡</td>
</tr>
<tr>
<td></td>
<td>−37.5 (−235 to 485), 0.718</td>
<td>−90 (−835 to 370), 0.754</td>
<td>(−115 to 265), 0.915</td>
</tr>
<tr>
<td>ΔPdetOmax H₂O, cm</td>
<td>−6 (−33 to 56), 0.194</td>
<td>−5 (−50 to 42), 0.509</td>
<td>(−12 to 11), 1.000</td>
</tr>
<tr>
<td>Qmax, ml/s</td>
<td>−0.5 (−35 to 9), 0.614</td>
<td>−2 (−15 to 22), 1.000</td>
<td>(−6 to 4), 1.000</td>
</tr>
<tr>
<td>ΔCompliance, ml/cm</td>
<td>−25 (−194 to 16), 0.002*</td>
<td>−27 (−250 to 37), 0.022*</td>
<td>(−37 to 35), 1.000</td>
</tr>
<tr>
<td>H₂O</td>
<td>Maximum cystometric</td>
<td>−105 (−555 to 50), 0.001*</td>
<td>(−120 to 145), 1.000</td>
</tr>
<tr>
<td>capacity, ml</td>
<td>Median (Range)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Two-sided P < 0.05 as statistically significant. † Within-group P value derived from the Wilcoxon signed rank test for within-patient preoperative–postoperative difference of each endpoint, with Bonferroni adjustment. ‡ Between-group P value from the Wilcoxon rank sum test for within-patient preoperative–postoperative difference, with Bonferroni adjustment. The 95% CI was constructed accordingly, but without Bonferroni adjustment.

CI = confidence interval; PdetOmax = detrusor pressure at maximum flow rate; PVR = postvoid residual; Qmax = maximum flow rate; TEA = thoracic epidural analgesia.
(patient-controlled analgesia), which could be a matter of future research.

In conclusion, thoracic epidurally administered bupivacaine (0.125%) alone or in combination with fentanyl (2 μg/ml) resulted in clinically relevant PVRs preoperatively and postoperatively. Epidurally administered fentanyl led to a more pronounced impairment of detrusor activity with a greater increase in PVRs. After open renal surgery, the storage phase was affected; however, the voiding phase was not further impaired. On the basis of our results, close attention to bladder function by monitoring of PVRs or transient catheterization during TEA is recommended. Methods to avoid or counteract the changes in voiding function during TEA should be a focus of further research.

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References
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