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# Transanal Endoscopic Operation under spinal anaesthesia

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## Abstract

### Background

Transanal Endoscopic Operation (TEO<sup>®</sup>) for rectal benign lesions and early rectal cancer may provide better oncological outcomes than flexible endoscopy. The major advantage of flexible endoscopy is that it does not require general anaesthesia. This prospective observational study assessed the feasibility and safety of TEO<sup>®</sup> performed under spinal anaesthesia.

### Methods

The study population comprised eligible consecutive patients who underwent TEO<sup>®</sup> under spinal anaesthesia with curative or palliative intent for rectal neoplasms larger than 20 mm in diameter or for recurrent lesions of any size. The primary endpoints were feasibility and safety; secondary endpoints were postoperative pain, as measured on a visual analogue scale, heart rate, systolic and diastolic BP, opioid requested, postoperative nausea or vomiting, and urinary retention.

### Results

The study included 50 patients (median age 70 years; 29 men and 21 women). No intraoperative complications occurred. The median duration of operation was 60 (range 20–165) min. No opioids were requested during the perioperative or postoperative period. The median postoperative pain score was 0 at 4, 8, 24 and 48 h after surgery. There were no significant fluctuations in heart rate, systolic and diastolic BP up to 48 h after the procedure ( $P = 0.379$ ,  $P = 0.386$  and  $P = 0.617$  respectively). Postoperative nausea and vomiting occurred in one patient, and urinary retention in four.

### Conclusion

TEO<sup>®</sup> under spinal anaesthesia was safe and feasible with no conversions to general anaesthesia.

## Introduction

Transanal endoscopic microsurgery (TEM) was introduced into clinical practice by Buess and colleagues[1] in 1983. Initial obstacles to its acceptance were the high cost of the instrumentation and difficulty in performing the technique without laparoscopic guidance. The development of piecemeal mucosectomy techniques (endoscopic mucosal resection, EMR) and, more recently, endoscopic submucosal dissection (ESD) have hindered its wider adoption. Today, the major advantage of flexible endoscopy is that it does not require general anaesthesia.

TEM is normally performed under general anaesthesia because of complex patient positioning and the length of the procedure, as the bowel is distended in preparation for surgery. With the recent introduction of Transanal Endoscopic Operation (TEO<sup>®</sup>) instrumentation (Karl Storz, Tuttlingen, Germany) and increasing experience with the technique, patient positioning has been simplified to either the prone or supine position, and the procedure duration has been shortened, even though the indications for TEM have been extended to include treatment of larger lesions[2]. This prompted the authors to evaluate the feasibility and safety of TEO<sup>®</sup> under spinal anaesthesia.

Lee and Lee[3] recently reported on transanal minimally invasive surgery for rectal tumours performed under spinal anaesthesia, but reports on use of regional anaesthesia in TEM or TEO<sup>®</sup> are currently lacking. This pilot study was conducted to assess the feasibility and safety of TEO<sup>®</sup> under spinal anaesthesia in the average fit patient, with a view to comparing regional and general anaesthesia in a future randomized clinical trial.

## Methods

This prospective observational study was conducted between 1 May 2014 and 30 April 2015 to collect data on eligible consecutive patients who underwent TEO<sup>®</sup>, with curative or palliative intent, for a rectal neoplasm larger than 20 mm in diameter or recurrent lesions of any size. Inclusion criteria were: informed consent, age 18–85 years, and American Society of Anesthesiologists fitness grade I–III. Exclusion criteria for spinal anaesthesia were: abnormal coagulation profile and previous surgery to the lumbar spine. The present study was registered at EudraCT (2015-002842-30).

An enema was given 2 h before surgery. Premedication comprised deep venous thrombosis prophylaxis and chlorphenamine (10 mg intramuscularly) 1 h before surgery. Antiallergic prophylaxis was given when indicated. Surgery was performed by one surgeon from a single team.

On arrival in the operating room, non-invasive monitoring was initiated comprising three-lead electrocardiogram (ECG), peripheral capillary oxygen saturation (SpO<sub>2</sub>), heart rate, and systolic and diastolic BP. Midazolam (1 mg) and antibiotic therapy (second-generation cephalosporin and metronidazole) were administered intravenously before inserting the rectoscope, and monitoring was continued for 24 h after surgery.

Patients were placed in the sitting position on the operating table, and a 25-G spinal needle was introduced into the subarachnoid space through the L2–L3 intervertebral space under aseptic conditions. After free flow of cerebrospinal fluid had been obtained, hyperbaric 2 ml bupivacaine 0.5 per cent was injected intrathecally. Patients were kept in the sitting position for 3 min and then positioned supine or prone, depending on the location of the neoplasm on the rectal wall and on the potential risk of peritoneal opening, in which case the patient was positioned prone to help maintain pneumorectum. After onset of anaesthesia, a urinary catheter was placed to keep the bladder empty. ECG, heart rate, systolic and diastolic BP, and SpO<sub>2</sub> were recorded at 5-min intervals during the procedure. Etilerfrine (2 mg) was administered intravenously if the mean systolic BP decreased by more than 20 per cent of the preanaesthesia baseline value.

The procedure was performed according to the standard technique described by Buess and colleagues[1] and using TEO<sup>®</sup> instrumentation[2] in combination with standard laparoscopic units (laparoscopic camera, endoscopic 300-W light source and conventional carbon dioxide thermal insufflators; Karl Storz). High-flow carbon dioxide insufflation at an endoluminal pressure of 8 mmHg was monitored and increased stepwise until sufficient bowel distension was obtained. A full-thickness rectal wall excision was performed with a monopolar hook and a standard electrothermal bipolar vessel sealing system at a distance of at least 5 mm from the neoplasm. The specimen was retrieved transanally. After the wall defect had been disinfected with iodopovidone solution, it was closed with one or more continuous sutures (Maxon<sup>™</sup> 3/0; Covidien, Dublin, Ireland) secured with silver clips (Richard Wolf, Knittlingen, Germany). At this stage, the endoluminal pressure was reduced to obtain better rectal wall compliance. Suturing was carried out with scrupulous attention to rectal lumen integrity; when suturing large defects, the surgeon placed a midline stitch to approximate the proximal and distal margins.

The duration of operation was recorded. The anaesthetist graded motor function by means of the Bromage scale, which assessed the intensity of motor block according to the patient's ability to move their legs[4, 5]. The length of time to reach a Bromage score of 2 was noted, at which point the patient was discharged to the ward. Patients were mobilized on the day of surgery. Pain was scored on a visual analogue scale (VAS) ranging from 0 to 5[6].

Intravenous paracetamol was used for analgesia, initiated during surgery and continued every 8 h, along with intravenous ketorolac (30 mg every 12 h for the first 24 h). Intravenous tramadol hydrochloride (100 mg) was used as rescue analgesia as needed (if the pain score measured on the VAS exceeded 3). Oral intake was allowed on the day of surgery. The urinary catheter was removed 24 h later, or at 48 h if the anterior wall was involved in the dissection. Patients were discharged from hospital if they were able to micturate and bowel movements had been restored, unless they developed a fever, postoperative pain or postoperative nausea and vomiting (PONV). Patients were contacted by telephone 15 days later, and asked to answer a questionnaire investigating the quality of their recovery and degree of satisfaction with the procedure.

The primary endpoints were the feasibility and safety of the procedure. Secondary endpoints were postoperative pain, as measured by VAS, heart rate, and systolic and diastolic BP at discharge from the operating room, then at 4, 8, 24 and 48 h after surgery, request for opioids (during and after operation), PONV and urinary retention. The Friedman test (non-parametric ANOVA for repeated measures) was used to detect a potential time trend in the repeated measures of heart rate, and systolic and diastolic BP.

## Results

Of 54 patients who met the inclusion criteria, four declined to participate in the study for personal reasons; none was considered ineligible for the study. Fifty patients (21 women and 29 men; median age 70 (range 36–85) years) were included in this pilot study (*Table 1*). The median diameter of the excised lesions was 34 (range 10–105) mm; the median lower margin from the anal verge was 5 (range 3–13) cm. Two lesions were circumferential. Preoperative histology revealed adenoma (39; 16 with low-grade and 23 with high-grade dysplasia) and adenocarcinoma (11); endoscopic ultrasonography staging was uT0 in 41 patients, uT1 in five and uT2 in four patients.

Table 1. Patient and tumour characteristics

**No of patients (*n* = 50)**

- \*

Values are median (range). EUS, endoscopic ultrasonography.

- †

Four T1sm1, one T1sm2, one T1sm3.

- ‡

All high-grade dysplasia.

Age (years)*	70 (36–85)
Sex ratio (M : F)	29 : 21
Tumour distance from anal verge (cm)*	5 (3–13)
Tumour diameter (mm)*	34 (10–105)
Lesions with diameter less than 20 mm	5
Preoperative histology	
Low-grade dysplasia	16
High-grade dysplasia	23
Adenocarcinoma	11
Preoperative EUS staging	
uT0	41
uT1	5
uT2	4
uT3	0
Patient position	
Prone	33
Supine	17
Duration of surgery (min)*	60 (20–165)
Postoperative histology and tumour stage	
Low-grade dysplasia	4
High-grade dysplasia	35
Tis	0
T1	6‡
T2	4
T3	1
R1 resection (tumour-free margin less than 1 mm)	3‡

Seventeen patients were treated in the supine and 33 in the prone position. Peritoneal opening in five patients was managed transanally by placing a double-layer suture. There were no intraoperative complications. The median duration of operation was 60 (range 20–165) min. No conversion to laparoscopy or general anaesthesia was required. No major anaesthesia-related events occurred during the procedure. The five patients in whom peritoneal opening occurred experienced abdominal discomfort that was treated by slightly reducing the endorectal carbon dioxide pressure and by administration of intravenous midazolam (1 mg) until complete subjective recovery. Another five patients who complained of abdominal discomfort also received intravenous midazolam (1 mg) until complete subjective recovery. Overall, three patients received intravenous midazolam at a dose of 3 mg, four at 2 mg and three at 1 mg. One patient whose procedure lasted 120 min complained of low back pain, which resolved with the administration of intravenous ketorolac (30 mg). Perioperative nausea in two patients resolved with the administration of intravenous ondansetron (4 mg).

The Bromage scale score was 1 in all patients at 2 h after returning to the ward; the median score on leaving the ward was 1.5 (range 1–2). No opioids were requested during the perioperative or postoperative period. There was no change up to 48 h after surgery in postoperative pain as assessed by VAS, heart rate, and systolic or diastolic BP (*Table 2*).

Table 2. Postoperative course

	<b>4 h</b>	<b>8 h</b>	<b>24 h</b>	<b>48 h</b>	<b><i>P</i>*</b>
• Values are median (range). VAS, visual analogue scale (range 0–5).					
• *					
Friedman test.					
Postoperative pain (VAS)	0 (0–5)	0 (0–4)	0 (0–4)	0 (0–3)	–
Heart rate (beats/min)	70 (50–98)	71 (50–110)	73 (52–101)	70 (53–99)	0.379
Systolic BP (mmHg)	130 (90–180)	130 (90–170)	125 (87–190)	130 (90–180)	0.386
Diastolic BP (mmHg)	73 (50–100)	75 (60–105)	70 (40–100)	73 (50–100)	0.617

Final histology showed adenoma with low-grade dysplasia in four patients, adenoma with high-grade dysplasia in 35, pT1 adenocarcinoma in 6 (4 sm1, 1 sm2, 1 sm3), pT2 adenocarcinoma in four and pT3 adenocarcinoma in one patient. Five patients with recurrent disease after piecemeal EMR had lesions smaller than 20 mm. Three patients, all with adenoma with high-grade dysplasia, had tumour-free lateral margins smaller than 1 mm. No endoluminal recurrence was observed at endoscopy at a minimum follow-up of 3 months.

All patients were mobilized within 12 h after returning to the ward. The urinary catheter was removed after 24 h in 17 patients and after 48 h in 33. Further catheterization was necessary in four patients because of urinary retention after removal of the first catheter. Oral nutrition was resumed 6 h after surgery and was well tolerated by all patients but one, who complained of PONV and received intravenous metoclopramide (10 mg twice in a single day). All patients were discharged from hospital after a median stay of 3 (range 2–14) days. Neither headache nor neurological sequelae were recorded. At the telephone follow-up interviews conducted 2 weeks after surgery, all patients but one said they were satisfied and would strongly recommend spinal anaesthesia. One patient was dissatisfied because of postoperative urinary retention.

One patient who underwent TEO<sup>®</sup> for a circumferential lesion required emergency surgery on postoperative day 9 to control major arterial bleeding below the surgical suture, which recurred after endoscopic management on day 3 and day 6. Emergency surgery was performed again with

TEO<sup>®</sup>, but this time under general anaesthesia. The second postoperative course was uneventful, and the patient was discharged 14 days after initial surgery.

## Discussion

This pilot study assessed the feasibility and safety of TEO<sup>®</sup> under spinal rather than general anaesthesia. It was speculated that TEO<sup>®</sup> under spinal anaesthesia could be done safely and effectively, with additional health benefits and a shorter operating room time than TEO<sup>®</sup> under general anaesthesia.

Traditionally, locoregional anaesthesia has been reserved for patients unfit for general anaesthesia, particularly those with severe chronic cardiopulmonary disease. Its use in healthy patients allows quicker recovery and reduces metabolic responses to surgical stress[7]. Combining a minimal access operation with segmental anaesthesia may further enhance the advantages of surgical dissection using TEO<sup>®</sup>.

More than 30 years ago, TEM revolutionized the technique and outcomes of transanal surgery, its indication rapidly extending from the treatment of large rectal adenomas[8, 9] to early rectal cancer[10]. More recently, its potential role in combination with neoadjuvant therapies for the treatment of more invasive cancer has been discussed[11-14]. The superiority of TEM over standard transanal surgery resides in the enhanced visualization and tissue manipulation that allow a more precise dissection. Its wider adoption has been limited, however, because of the steep learning curve to master the technique and because it is performed only under general anaesthesia; these two factors have favoured the use of EMR, despite its associated recurrence rate at 3 months of more than 10 per cent for benign lesions[15] and more than 10 per cent for invasive cancers[16]. It is impossible reliably to determine the type and stage of a large sessile rectal tumour before surgery, and *en bloc* resection should be undertaken when possible. Moreover, ESD has failed to provide results comparable to those of TEM for flexible endoscopy, and the R0 resection rates differ considerably between the two: 75 per cent with ESD *versus* 90 per cent with TEM[17].

Besides oncological efficacy, cost-effectiveness is playing an increasingly critical role in the therapy decision-making process. A surgical procedure that does not require general anaesthesia can be expected to provide early recovery and an oncologically correct excision of the tumour with minimal invasiveness. The present results have demonstrated the feasibility and safety of undertaking TEO<sup>®</sup> under spinal anaesthesia in a prospective series of consecutive patients. TEO<sup>®</sup> was undertaken safely under spinal anaesthesia using insufflation pressures of 8 mmHg up to the minimum pressure to obtain sufficient and stable distension of the rectum. No adverse anaesthesia-related events were recorded, postoperative pain was limited and there was a high level of patient satisfaction with spinal anaesthesia. Neither peritoneal opening, nor circumferential lesions, nor invasive cancers up to pT3 posed a contraindication to complete TEO<sup>®</sup> under spinal anaesthesia in this series, and procedures lasting up to 165 min could be completed safely. One patient required emergency surgery for persistent arterial bleeding, which was not related to the type of anaesthesia. Nevertheless, intraperitoneal, circumferential or advanced malignant lesions should be evaluated scrupulously on an individual basis, as further studies are required to demonstrate whether they should be considered contraindications to spinal anaesthesia.

Controlled ventilation during laparoscopic operations performed under spinal anaesthesia has been recommended[18], owing to factors that may induce hypercapnia, such as absorption of carbon dioxide throughout the peritoneum and impairment of ventilation due to abdominal distension. Respiratory difficulty is a common problem with spinal anaesthesia in the presence of abdominal distension, for which assisted masked ventilation is recommended. Nevertheless, this was not a

concern here, possibly owing to the relatively short duration of surgery and/or the limited bowel distension, particularly in patients who underwent surgery in the prone position.

The occurrence of PONV is more common after general anaesthesia than after spinal anaesthesia, and was experienced by only one patient in the present series. Urinary retention associated with regional anaesthesia[19] owing to interruption of the micturition reflex has been reported in up to 23 per cent of operations[20]; however, only four patients in this series required continued catheterization.

The possibility of avoiding the use of general anaesthesia, even in more challenging procedures, opens new opportunities for TEO<sup>®</sup>, for example during transanal local excision in patients judged unfit for general anaesthesia. In the present study, postoperative pain was acceptable, and heart rate and BP did not change remarkably during the 48 h after surgery. Although the study did not include a comparative group, it is reasonable to assume that these parameters would have been considerably different in the early postoperative period after general anaesthesia. Although not using general anaesthesia should result in earlier discharge from hospital, the authors thought it wise to follow their usual protocol for the duration of this pilot study. Based on the good results, it is planned to shorten the hospital stay, at least for asymptomatic patients undergoing extraperitoneal excisions.

Although comparative studies are awaited to verify the real effectiveness of the two techniques, the present study provides evidence that transanal minimally invasive surgery and also TEO<sup>®</sup> can be performed safely under spinal anaesthesia. This opens new perspectives, with a possible advantage over flexible endoscopy techniques. As confidence with the use of transanal platforms for endoscopic surgery increases, the use of transanal total mesorectal excision, the technique of choice for treating very low rectal cancers, can be expected to grow. Based on the encouraging results of this pilot study, a prospective randomized trial is in progress to compare locoregional and general anaesthesia, in terms of postoperative pain, complications, recovery and patient satisfaction, including quality-of-life assessment.

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