ORIGINAL ARTICLE

Topography of the extrinsic internal anal sphincter nerve supply during laparoscopic-assisted TAMIS TME: five key zones of risk from the surgeons' view

Werner Kneist · Andreas D. Rink · Daniel W. Kauff · Moritz A. Konerding · Hauke Lang

Abstract

Purpose Sparing the extrinsic autonomic innervation of the internal anal sphincter during total mesorectal excision is important for the preservation of anal sphincter function. This study electrophysiologically confirmed the topography of the internal anal sphincter nerve supply during laparoscopic-assisted transanal minimally invasive surgery for total mesorectal excision.

Methods This prospective study was conducted at two large multispecialty referral centers. Six patients (five males and one female) aged between 45 and 65 years with low rectal cancer (≤5 cm from the anal verge) were enrolled. Surgery was performed under electric stimulation of the pelvic autonomic nerves with observation of the electromyographic signals of the internal anal sphincter.

Results The minimally invasive transanal surgical approach enabled advantageous visualization of the pelvic autonomic nerves in all patients. In particular, extrinsic innervation to the internal anal sphincter near the levator muscle was consciously spared under electrophysiological confirmation. The evoked absolute electromyographic amplitudes of the internal anal sphincter during transanal minimally invasive surgery were significantly lower than the initial results of the laparoscopic approach [3.7 μV (interquartile range 2.4; 5.7) vs.

4.3 μV (interquartile range 3.1; 8.6); $p=0.002$]. Five key zones of risk for pelvic autonomic nerve damage were identified. No complications occurred.

Conclusions The electromyographic results of this preliminary study indicate advantages for sparing the internal anal sphincter innervation during transanal minimally invasive mesorectal dissection considering the specific in situ neuroanatomical topography.

Keywords Rectal cancer · Minimally invasive · Transrectal · Autonomic nervous system · Intraoperative monitoring · Internal anal sphincter

Introduction

Sphincter-preserving surgery with coloanal anastomosis for low rectal cancer is technically challenging, especially in cases of supra-anal (type I) and juxta-anal (type II) tumors [1]. In addition to oncological radicalness, the maintenance of sufficient function of the anal sphincter complex must be ensured by an operative procedure in order to achieve reasonable continence after this type of surgery. In earlier trials, we found that the anal resting tone after surgery is the major determinant of continence after restorative proctectomy [2]. A tumor distance from the anal ring greater than 1 cm and anastomosis higher than 2 cm above the anal verge have been identified by other authors as independent predictors of good continence after intersphincteric resection [3].

The significant role of the internal anal sphincter (IAS) in fecal continence was clarified by Stelzner et al. [4, 5]. Disturbances in continence were found to occur with IAS denervation, especially after a pull-through procedure, despite preserved external anal sphincter function. In 1951, Otto Goetze reported that extrinsic nerve fibers that emerge from the distal part of the ganglion pelvinum branching to the IAS are at high

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risk during anterior rectal resection. Goetze created many indicative drawings and presumed that a "down-to-up" procedural concept may offer advantages in terms of sparing the IAS innervation [6].

With the recent introduction of transanal minimally invasive surgery (TAMIS) total mesorectal excision (TME), pelvic autonomic nerve preservation may be possible [7]. The procedure combines "up-to-down" and down-to-up surgery and seems to improve visualization and spare the pelvic splanchnic nerves (nerve fibers originating from segments S2–S5), inferior hypogastric plexus (IHP), and neurovascular bundles during transanal endoscopic dissection [7–12]. However, the nerve-sparing potential of the down-to-up procedure with regards to the extrinsic innervation of the IAS has not yet been taken into consideration.

Intraoperative electrophysiological pelvic neuromonitoring allows the identification and verification of autonomic nerve function and is a surrogate parameter for functional outcome [13, 14]. Especially during minimally invasive procedures, selective stimulation of extrinsic supralevatoric neurogenic pathways to the IAS is feasible [15, 16].

The present study evaluated the nerve-sparing potential of the transanal approach of laparoscopic-assisted TAMIS TME using electrophysiological confirmation of the extrinsic IAS nerve supply with specific focus on the in situ neuroanatomical topography.

Materials and methods

Laparoscopic-assisted TAMIS TME

A consecutive series of six highly selected patients with low rectal cancer undergoing ultra-low anterior resection were enrolled prospectively at two centers (two patients from Leverkusen General Hospital and four from University Medical Center). Diagnosis, staging, and indication for laparoscopic-assisted TAMIS TME were discussed in a colorectal-specific multidisciplinary tumor conference. In the case of neoadjuvant chemoradiotherapy, only patients with a good clinical response were enrolled. In all procedures, electrophysiologically controlled rendezvous transanal and laparoscopic nerve-sparing TME was performed by two experienced colorectal surgeons. Written informed consent for surgery and intraoperative functional electrophysiological testing was obtained from all patients. Patient and tumor characteristics and the surgical and histopathological results are summarized in Table 1.

Surgery was performed in lithotomy position under total intravenous anesthesia. For the conventional laparoscopic approach, three to five trocars were inserted. After mobilization of the splenic flexure, high tie of the inferior mesenteric artery, and central ligation of the mesenteric vein, the peritoneal fold was opened circumferentially. The nerve-sparing procedure started from up to down with posterior mesorectal dissection, followed by lateral, anterolateral, and anterior dissection down to the level of the midrectum.

For the transanal part of the procedure, a Lone Star Retractor (CooperSurgical, USA) was applied. The rectum was flushed with povidone-iodine solution (Betaisodona®). For supra-anal cancer (type I), a handheld (Parks) retractor was used, enabling a circumferential full-thickness incision of the rectal wall by electrocautery. The incision was located above the dentate line in patients with supra-anal lesions, preserving the IAS and achieving a ≥1-cm distal resection margin. In the case of type II low rectal cancer (juxta-anal lesions), the incision was made at the level of the dentate line in order to perform a partial intersphincteric resection (pISR) of the IAS.

After closing the oral rectal orifice with a purse-string suture, the perineal cavity was rinsed with a cytocidal agent. A circumferential full-thickness rectal transection was carried out until reaching the mesorectal plane. A multiport device (SILS™® Port; Covidien, Inc., Norwalk, CT, USA, for cases 1 and 2; GelPOINT® path transanal platform; Applied Medical, European Union, for cases 3 to 6) was inserted. CO_2 was continuously insufflated to a pressure of 9–14 mmHg. A 30° angled laparoscope (K. Storz, Tuttlingen, Germany) was used. Further mesorectal dissection was extended transanally from down to up. The procedure started posterior and moved forward in the posterolateral, lateral, anterior, and anterolateral directions. Rectal mobilization was completed if the approach from above was reached circumferentially. In all cases, the specimen was removed transanally. The colonic resection was performed extracorporally. Finally, all patients underwent ileostomy creation.

Electrophysiological confirmation of extrinsic pelvic autonomic innervation

Neurogenic pathways were identified and traced by electric stimulation with a bipolar microfork probe under simultaneous electromyography (EMG) of the IAS and cystomanometry (Inomed Medizintechnik GmbH, Emmendingen, Germany). For EMG, bipolar needle electrodes were inserted into the IAS and external anal sphincter (Fig. 1). The methodological setup was described in detail elsewhere offering an accurate prediction of postoperative ano(-neo)rectal and urinary function [14]. Repetitive bipolar electric stimulations were carried out sequentially on both pelvic sides for neuromapping during up-to-down and down-to-up mesorectal dissection. A current of 6 mA, a frequency of 30 Hz, and a monophasic rectangular pulse duration of 200 μs were used in all operations. Consecutive stimulation-dependent unilateral or bilateral increases in the EMG amplitude (V) of IAS were rated as positive stimulation, indicating a preserved extrinsic nerve supply.

Table 1 Patient characteristics and intraoperative and histopathological results of laparoscopic-assisted transanal minimally invasive surgery (TAMIS) total mesorectal excision (TME)

Patient no.	Sex	Age (years)	BMI (kg/m^2)	ASA[a]	Tumor site (cm)[b]		Procedure	Anastomosis		M.E.R.C.U.R.Y. graduation	TNM stage	LN ratio
					From AV	From DL		cm from AV	Technique			
1	M	45	22.9	I	5	2	pISR	2	Stapled J-pouch	I°	ypT0N0M0R0[c]	0/9
2	F	56	23.8	I	4.5	1.5	pISR	2	Hand-sewn J-pouch	I°	pT1N1M0R0	1/18
3	M	49	24.9	II	5	3	CAA	2.5	Hand-sewn J-pouch	I°	pT1(sm1)N1bM0R0	2/15
4	M	60	24.4	II	5	3	CAA	3	Hand-sewn E-to-E	I°	ypT3N2bM1(Hep)R2[d]	24/32
5	M	65	24.9	II	4.5	0.5	pISR	3	Hand-sewn S-to-E	I°	ypT0N0M0R0[c]	0/13
6	M	61	28.1	II	3	0	pISR	2	Hand-sewn E-to-E	I°	ypT0N0M0R0[c]	0/4

M male, *F* female, *BMI* body mass index, *AV* anal verge, *DL* dentate line, *pISR* partial intersphincteric resection, *CAA* coloanal anastomosis, *S-to-E* side to end, *E-to-E* end-to-end, *LN* lymph node

[a] Perioperative risk assessment according to the American Society of Anesthesiologists

[b] Assessed before a long-course chemoradiotherapy

[c] Long-course chemoradiotherapy

[d] Only chemotherapy, free distal and circumferential resection margins

Down-to-up neuroanatomical topography

During the down-to-up procedure, macroscopic and electrophysiological observations of the in situ topography of the nerve supply to the IAS were documented. Exclusive situations were photographed. The documentation was reviewed by an anatomist in order to describe the neurogenic pathways from the down-to-up point of view.

Statistical analysis

Statistical analyses were performed using SPSS® version 20.0 (SPSS, Chicago, IL, USA). The Wilcoxon signed-rank test was used to compare the intraoperative absolute EMG signals in regards to the increase in amplitude. The Mann-Whitney *U* test was used to compare the absolute evoked EMG amplitudes during laparoscopic and transanal minimally invasive mesorectal dissection. Results were expressed as median and interquartile range (IQR). A value of $p < 0.05$ was considered significant.

Results

Electrophysiological results

The bipolar microfork probe designed for laparoscopic neurostimulation was easily inserted through the multiport device, enabling flexible bilateral neuromapping during transanal mesorectal dissection. The neuromapping resulted in evoked absolute EMG amplitude increases in the IAS during the laparoscopic [resting EMG values 1.6 μV (IQR 1.3; 2.0) vs. evoked EMG values 4.3 μV (IQR 3.1; 8.6); $p < 0.001$] and transanal approaches [resting EMG values 0.9 μV (IQR 0.6; 1.4) vs. evoked EMG values 3.7 μV (IQR 2.4; 5.7); $p < 0.001$]. The median absolute resting and evoked EMG amplitudes were significantly lower during the down-to-up procedure than during the up-to-down procedure ($p = 0.002$ and $p < 0.001$).

The extrinsic supralevatoric IAS innervation was confirmed bilaterally in all six patients during the up-to-down mesorectal dissection. Subsequent electrophysiologically controlled transanal down-to-up dissection (Figs. 2 and 3)
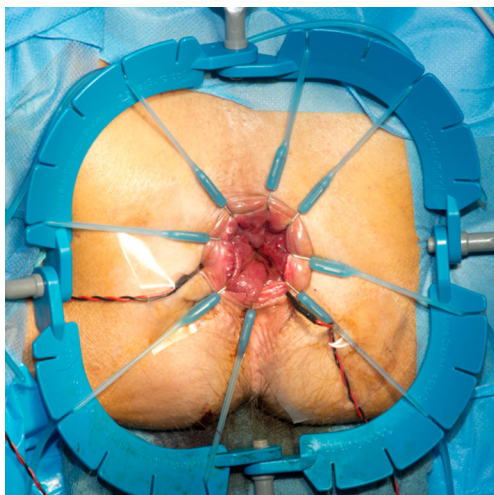

Fig. 1 Bipolar electromyographic electrodes inserted into the internal anal sphincter at 5 o'clock lithotomy position and external anal sphincter at 8 o'clock lithotomy position
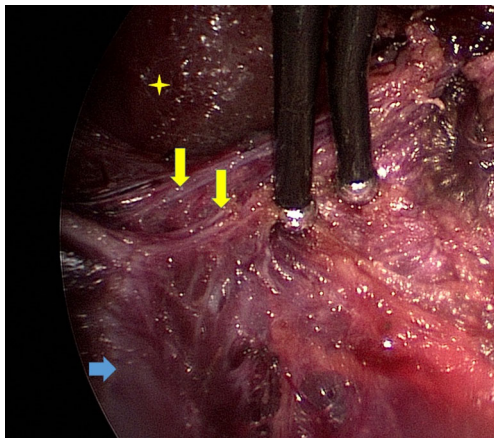
Fig. 2 Bipolar electrical stimulation slightly above IAS level (*blue arrow*) at 8 o'clock lithotomy position for verification of extrinsic innervation (*yellow arrows*). *Yellow star* levator ani muscle

revealed bilateral preservation in four patients and unilateral preservation of the IAS innervation in one patient undergoing pISR (case 2, Table 1). In one patient, electrophysiological testing during the down-to-up dissection was not performed (case 6, Table 1). According to the tumor located 3 cm from the anal verge at the dentate line, the intersphincteric resection was carried out approximately 1 cm below the dentate line. Thereby, almost 50 % of the IAS had to be sacrificed and further electrophysiological testing was not possible (Fig. 4).

Key zones of risk for autonomic nerve damage during TAMIS mesorectal dissection

During TAMIS, five key zones where pelvic autonomic nerves are at risk for damage were identified (Fig. 5). No complications did occur.
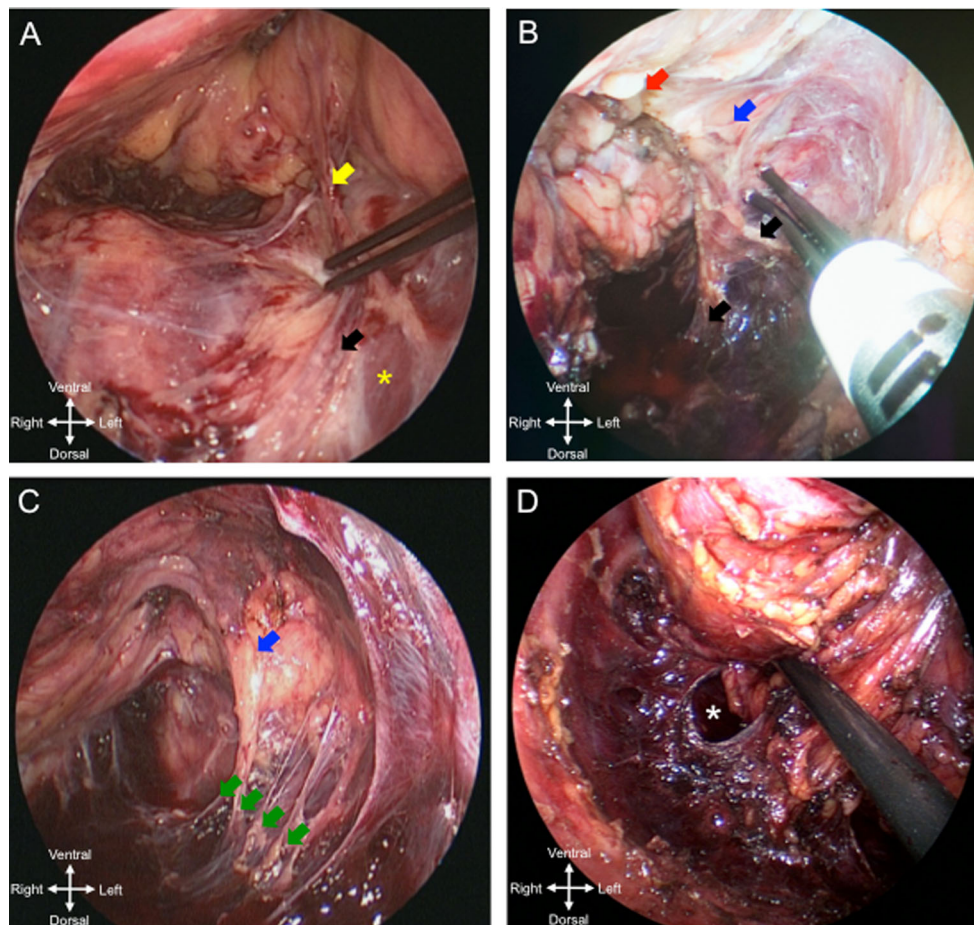

Fig. 3 Surgical situs during transanal mesorectal dissection (**a–d**). Electrophysiological identification and functional verification of neurogenic pathways to the internal anal sphincter after posterolateral transanal mesorectal dissection performed with a bipolar microfork probe. The nerve fibers emerge from the posterior-inferior edge of the inferior rectal plexus (*yellow arrow*) and head to the internal anal sphincter (*black arrow*) at the level of the levator ani muscle (*yellow star*) (**a**). Further lateral and anterolateral dissection revealed the inferior aspect of the inferior hypogastric plexus (*blue arrow*) with its anterior portion

branching to the genitals as neurovascular bundles (*red arrow*) and its posterior-inferior portion branching to the internal anal sphincter (*black arrows*) (**b**). Further ongoing transanal posterior mesorectal dissection revealed the pelvic splanchnic nerves (*green arrows* mark the ventral branches of the sacral spinal nerves) most likely at the level of sacral nerves S5 to S3, located posterolateral and running along the lateral pelvic sidewall to form the inferior hypogastric plexus (*blue arrow*) (**c**). Rendezvous at the level of midrectum with the "up-to-down" procedure (*white star*) (**d**)
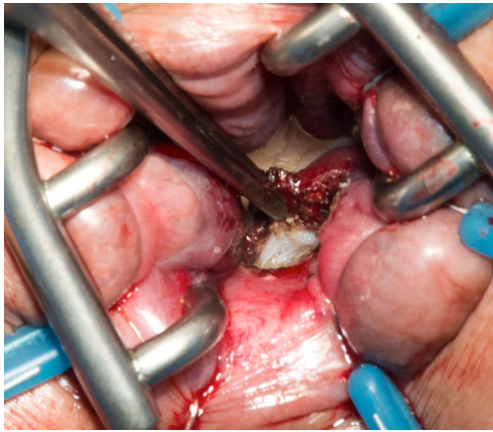
Fig. 4 Circumferential intersphincteric incision by electrocautery. The incision was located 1 cm below the dentate line in a patient with a tumor located 3 cm above the anal verge at the dentate line. Part of the internal anal sphincter (white muscle tissue) is exposed

Key zone 1   The first key zone is the circumferential resection of the rectal wall or the oral IAS at the level of the upper intersphincteric space, especially when an incision is performed at or below the dentate line.

Key zone 2   Dissection started posteriorly and proceeded cephalad in the avascular plane. Neither macroscopic assessment nor electrophysiological testing identified autonomic nervous tissue in that area. The extrinsic supralevatoric neurogenic pathways to the IAS were identified initially during electrophysiologically controlled posterolateral dissection corresponding to 4–5 and 7–8 o'clock lithotomy position at the level of the levator ani muscle, which is the second key zone.

Key zone 3   Lateral dissection allowed electrophysiologically guided tracing of the nerve fibers from posterolateral to anterolateral and to their origin from the posterior-inferior edge of the inferior rectal plexus located laterally on the pelvic sidewall at 3 and 9 o'clock lithotomy positions above the level of the levator ani muscle, the third key zone.

Key zone 4   The fourth key zone is the further cephalad posterolateral dissection, which enabled the identification of the pelvic splanchnic nerves at the level of sacral nerves S4 and S3. Electrophysiological neuromapping resulted in evoked EMG amplitudes.

Key zone 5   The fifth key zone is the anterolateral dissection, which revealed the IHP with its anterior parts

Fig. 5 Schematic drawing of key zones 1–5, where autonomic nerves are ▶ at risk during transanal approach (surgeon's view is limited to the left hemipelvis)

Key zone 1

Key zone 2

Key zone 3

Key zone 4

Key zone 5
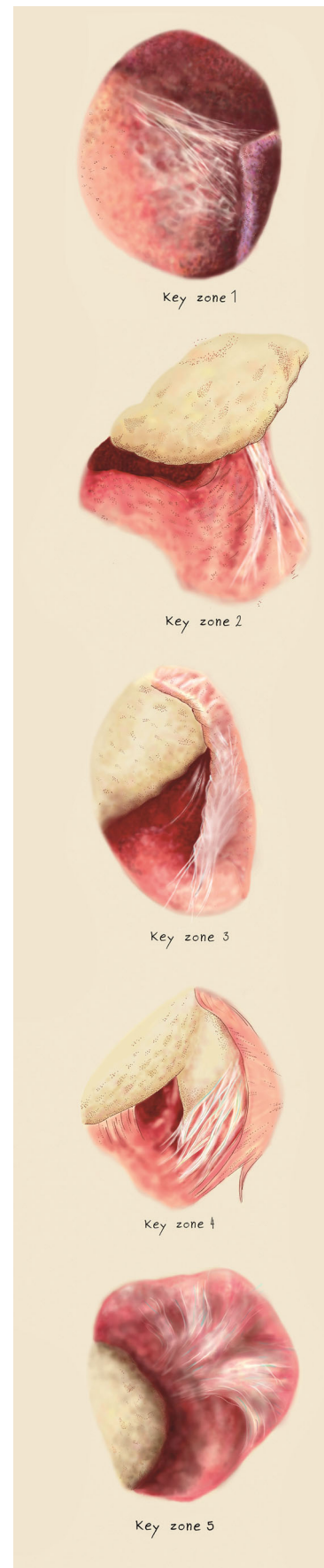
emerging from the inferior edge and heading to the genitals as the neurovascular bundles at 2–3 and 10–11 o'clock lithotomy positions at the level of the prostate (vagina).

Discussion

Besides an investigation of the oncological safety of TAMIS TME [17], the nerve-sparing potential of this transanal approach needs to be examined as objectively as possible. In this context, the extrinsic nerve supply to the IAS remains highly topical.

The IAS denervation could be electrophysiologically demonstrated to occur at the level of the pelvic floor in the case of abdominoperineal resection. In two patients without confirmed intact extrinsic innervation at the end of a sphincter-saving TME, IAS palsy was assessed later [13]. Surgeons are requested to remain attentive to actual anatomical investigations of nerves supplying the IAS. Today's drawings are highly intriguing and based on detailed topographical anatomy, conventional staining, immunohistochemistry, and three-dimensional reconstructions [18–21]. Laparoscopic visualization could overcome some of the boundaries for the identification and functional verification of neural tissue, even in the depth of the minor pelvis that is poorly accessible in open procedure. Compared to open procedure, the evoked EMG signals in the IAS were significantly higher during laparoscopic surgery, which clearly indicates a more selective nerve-sparing potential [16]. However, preparation at long distances with rigid instruments in a narrow pelvis or bulky mesorectum and difficult stapling maneuvers frequently jeopardize the preservation of IAS innervation, even in laparoscopy. Defining the aboral resection margin as the first step in the down-to-up procedure could eliminate the risk of deteriorating oncological outcome, especially in patients with very low rectal cancer [22]. Hypothetically, TAMIS TME has a more advantageous nerve-sparing effect.

In the present study, the TAMIS approach was found to offer excellent visualization of the deep pelvic cavity. However, five key zones of risk for nerve damage were identified.

The first key zone is the circumferential incision of the rectal wall at the level of the upper intersphincteric space. A partial resection of the IAS is performed by starting the transanal procedure with an incision at the level of the dentate line. Interindividual differences in the surgical length (range 3.0–5.3 cm) and anatomical length (range 1.0–3.2 cm) of the anal canal have to be considered [23], especially in cases such as patient 6 in the present study. However, the function of the IAS could still be preserved, as it is dependent on the innervation rather than the amount of preserved muscle tissue [2,

24]. With diameters of 0.1 mm, the intersphincteric nerves contain a mixture of sympathetic and parasympathetic nerve fibers embedded in fatty tissue, which tend to run along the internal, rather than the external, anal sphincter [19]. Therefore, injections to enhance tissue volume and careful preparation should be the method of choice.

The second key zone is the posterolateral mesorectal dissection, revealing terminal efferents to the IAS at 4–5 and 7–8 o'clock lithotomy positions. These nerve fibers could be macroscopically identified by electrophysiological tracing along the superior fascia of the levator ani muscle. Similar results were found by laparoscopic neuromapping for other applications [15, 16]. Kinugasa et al. demonstrated in ten cadavers that the major autonomic nerve input to the IAS originates from the inferior rectal plexus, a secondary plexus of the IHP, rather than from the lower rectum [20].

The third key zone is the transanal lateral mesorectal dissection, which revealed the tortuous cephalad course of these nerves with their origin from the inferior aspect of the IHP. The in situ findings are in accordance with novel three-dimensional neuroanatomical reconstructions describing the posterocaudal direction of the inferior rectal plexus [19].

The fourth key zone is further posterolateral mesorectal dissection reaching the level of sacral nerves S4 and S3, enabling macroscopic and electrophysiological identification of the pelvic splanchnic nerves.

The fifth key zone is the transanal anterolateral mesorectal dissection. Neurovascular bundles emerging from the lower anterior part of the IHP with an anteroinferior direction to the genitals were identified. In cadavers, the origin of the lower rectal branches was found at the posterolateral corner of the prostate or on the posterolateral side of the vagina (or the lower posterior paracolpium) [21]. The revealed areas at 2–3 and 10–11 o'clock lithotomy positions at the level of the distal rectum have been reported to be nerve-rich zones [20]. Stimulation of this region (IHP) led to positive results for IAS EMG.

In the present study, only one of the three patients undergoing pISR under electrophysiological testing had a unilateral negative EMG result, indicating iatrogenic damage to the neural supply of the IAS, probably within the first or second key zone during TAMIS due to the mandatory radicalness in the case of a unilateral tumor. However, according to a previous investigation, severe functional impairment is more likely to occur after bilateral electrophysiologically confirmed nerve damage [14]. In patient 6, the EMG-based electrophysiological testing during the down-to-up procedure was not possible due to the necessity of performing the incision below the dentate line, which resulted in sacrifice of almost 50 % of the IAS.

In the presented series, three patients underwent J-pouch anastomosis, one patient side-to-end anastomosis, and two patients end-to-end anastomosis. With regard to anorectal

functional outcome, this has to be taken into account beside the occurred iatrogenic nerve lesion.

Sylla and co-workers first highlighted functional outcomes by demonstrating transient major urinary dysfunction in two of five rectal cancer patients undergoing TAMIS TME. In addition to fecal incontinence and sexual dysfunction, the neurogenic bladder has to be assessed from the very beginning [11, 25].

Although not in the scope of the present study, four of the six patients had bilateral positive neuromapping results with cystomanometry. In one patient (case 5, Table 1), bladder innervation was only unilaterally confirmed on the same pelvic side during laparoscopic and transanal dissection. This finding could be attributed to neoadjuvant long-course chemoradiotherapy, which may lead to nerve tissue damage in the irradiated area. In another case, a former stimulation-induced bilateral increase in intravesical pressure during laparoscopy became unilaterally negative after the final transanal neuromapping, indicating nerve damage during key zones 4 and 5 (case 4, Table 1). However, the postoperative ultrasound measurements of post-void residual urine volumes were <50 ml in each case.

Finally, the comparison of absolute EMG amplitudes of the IAS during the down-to-up procedure and the up-to-down procedure may be of interest, as it revealed significant lower resting and evoked amplitudes during TAMIS. This difference may be attributed to anal stretching by the multiport device. Horgan and co-workers already reported such a phenomenon, demonstrating that intramural stretching caused partial anal hypotonia and injury to the IAS [26].

The study is limited to the intraoperative macroscopic and electrophysiological findings in six rectal cancer patients. Stoma has just been closed in all patients. Data on anorectal function have not yet been evaluated.

In conclusion, the TAMIS approach provides excellent access to the extrinsic autonomic nerves responsible for the maintenance of IAS function after ultra-low anterior resection. The combination with electrophysiological neuromapping may offer the verification of the functional nerve integrity and serve as a method for detection of unrecognized nervous tissue. Description of variations of the course of pelvic autonomic nerves between individuals in terms of architecture and identifiability observed by the transanal approach should be addressed to investigations in larger study populations. Further clinical investigations including functional outcome are mandatory in order to demonstrate that the procedure could provide the benefit of sparing IAS innervation when considering the specific in situ neuroanatomical topography and key zones of risk of pelvic autonomic nerve damage.

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