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ORIGINAL ARTICLE

Continuous intraoperative monitoring of autonomic nerves during low anterior rectal resection: an innovative approach for observation of functional nerve integrity in pelvic surgery

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Abstract
Purpose The aim of this study was to develop a methodological setup for continuous intraoperative neuromonitoring with intent to improve nerve-sparing pelvic surgery.
Methods Fourteen pigs underwent low anterior rectal resection. Continuous stimulation of pelvic autonomic nerves was carried out with a newly developed tripolar surface electrode during lateral, anterolateral, and anterior mesorectal dissection. Neuromonitoring was performed under electromyography of the autonomic innervated internal anal sphincter.
Results Continuous neuromonitoring resulted in significantly increased electromyographic amplitudes of the internal anal sphincter, confirming intact innervation throughout the whole dissection in each animal (median 0.9 μV, interquartile range 0.5; 1.5 vs. median 3.4 μV, interquartile range 2.1; 4.7) ($p<0.001$). The median dissection time in each animal was 10 min within a median number of ten (range 8–13) tripolar electric stimulations.
Conclusion The present study is the first to demonstrate that continuous intraoperative monitoring of pelvic autonomic nerves during low anterior rectal resection is feasible.

Keywords Intraoperative monitoring · Autonomic nerves · Electric stimulation · Electromyography · Anal sphincter · Rectal cancer

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Introduction

Although the introduction of total mesorectal excision improved patients' prognosis and quality of life, surgery for rectal carcinoma is still associated with increased rates of urinary and sexual dysfunction [1]. Furthermore, it was shown that total mesorectal excision could also result in newly developed fecal incontinence [2], which is one characteristic factor of the so-called anterior resection syndrome. Neurogenic incontinence could be attributed to the intraoperative denervation of the internal anal sphincter [3], which accounts for approximately 52–85% of the anal resting pressure [4].

To improve nerve-sparing pelvic surgery, intermittent intraoperative neuromonitoring was introduced in several surgical disciplines. Different techniques have been described previously using penile tumescence, intracavernous, intraurethral, or intravesical pressure measurement [5–9]. It has been demonstrated that intermittent neuromonitoring objectifies the macroscopic assessment of autonomic nerve integrity and is applicable for risk assessment and secondary prevention of function disturbances after total mesorectal excision [10]. In a recent animal study, intermittent

intraoperative neuromonitoring has been performed under electromyography of the autonomic innervated internal anal sphincter with promising results [11]. Further developments of this new method were carried out to improve the reliability of the stimulation-induced internal anal sphincter electromyographic signals [12]. Initial results of a clinical study demonstrated that intermittent neuromonitoring under electromyography of the internal anal sphincter is feasible in rectal cancer patients [3].

Generally, intermittent intraoperative neuromonitoring is associated with alternating stimulation sites and thus variable neuromonitoring signals. It also leads to repetitive interruptions of the surgical preparation and larger time intervals between two stimulations during which unobserved nerve injury could occur. To overcome these shortcomings, the development of a continuous intraoperative neuromonitoring is desirable. In pelvic surgery, the complexity of topography, functional neuroanatomy [13–15], and standardized oncologic procedures placed high demands on a methodological setup for continuous intraoperative neuromonitoring. After the development of a suitable electrode design [16], the aim of this experimental study was to realize a continuous intraoperative monitoring of pelvic autonomic nerves under electromyography of the internal anal sphincter.

Materials and methods

Surgical procedure

Fourteen consecutive male pigs (German Landrace; Animal Breeding Farm, Zornheim, Rhineland-Palatinate, Germany), weighing in median 28 kg (range 27–31), underwent a standardized nerve-preserving low anterior rectal resection. Sharp dissection started posteriorly and moved forward with lateral, anterolateral, and anterior mesorectal dissection. This was followed by low rectal resection. Intravenous anesthesia was used as previously described [11]. After the operations, animals were sacrificed with an overdose of thiopental sodium and 40 ml KCl 7.45% i.v. The experiments were approved by the local authorities (Regional Board of Animal Welfare, Koblenz, Rhineland-Palatinate, Germany).

Neuromonitoring setup

According to a previous study [12], electromyography of the internal anal sphincter was carried out with a bipolar needle electrode. The ground electrode was placed on the left thigh. The processed electromyographic activity of the internal anal sphincter (amplitude in V) was observed throughout the surgical procedure with a neuromonitoring system (NeMo®, Neuroexplorer® version 4.3, Inomed Medizintechnik GmbH, Emmendingen, Germany).

Intermittent stimulation of the pelvic autonomic nerve was performed with a handheld bipolar microfork probe. Stimulation-induced sequential amplitude increases of the internal anal sphincter electromyographic signal were considered as positive response.

Continuous intraoperative neuromonitoring

After opening of the peritoneal fold and posterior mesorectal dissection, the pelvic splanchnic nerves were identified by means of intermittent electric stimulations (Fig. 1). For continuous intraoperative neuromonitoring, the newly developed tripolar surface electrode (IKONA-B1-IKB1, IKONA-consortium, Germany) was applied on the stimulation site with the highest recorded electromyographic amplitude increase (Fig. 2). In each operation, continuous stimulation started on the right pelvic side and consisted of repeated pulse trains of 30 s. Interval between the stimulations was 30 s. Current of 9 mA, frequency of 30 Hz, and monophasic rectangular pulses with pulse durations of 200 μs were chosen. Continuous intraoperative neuromonitoring was performed bilaterally during all steps of mesorectal dissection (Fig. 3). After low anterior resection, autonomic innervation was finally verified by bilateral intermittent neurostimulation.

Data analysis

The intraoperative assessment of neuromonitoring signals was carried out by a surgeon. The acquired data were additionally analyzed in MATLAB (Version 7.7.0.471, The MathWorks, Inc., Natick, MA, USA) in order to examine the recorded electromyographic amplitudes. Statistical

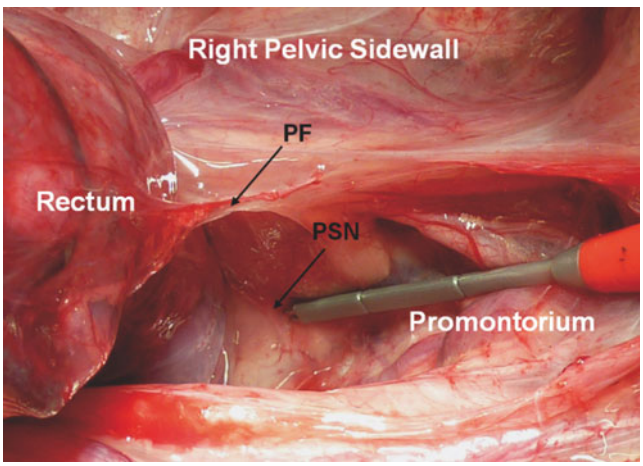

Fig. 1 Pelvic autonomic nerve mapping after posterior mesorectal dissection. *PF* peritoneal fold, *PSN* pelvic splanchnic nerves

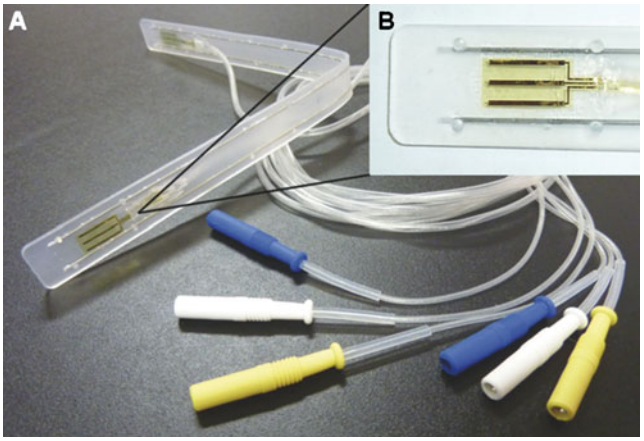

Fig. 2 Tripolar surface electrodes (polyimid and gold layers) on both ends of a V-shaped electrode holder (*A*). Magnified image of the electrode with silicone knobs and rigid wires (*B*)

analysis was carried out with SPSS® version 18.0 (Statistical Package for Social Sciences program, Chicago, IL, USA). Wilcoxon's signed rank test was used for determining statistically significant differences of neuromonitoring signals. Results were expressed as median and interquartile range. $P<0.05$ was considered as statistically significant.

Results

A median number of three (range two–five) intermittent neurostimulations was mandatory in order to detect reliable stimulation sites for application of the tripolar surface electrode. In all animals, continuous intraoperative monitoring of autonomic nerves during low anterior rectal resection was successfully realized with adequate stimulation results. In one pig, the tripolar surface electrode was dislocated in a stimulation-free interval during left anterolateral dissection.

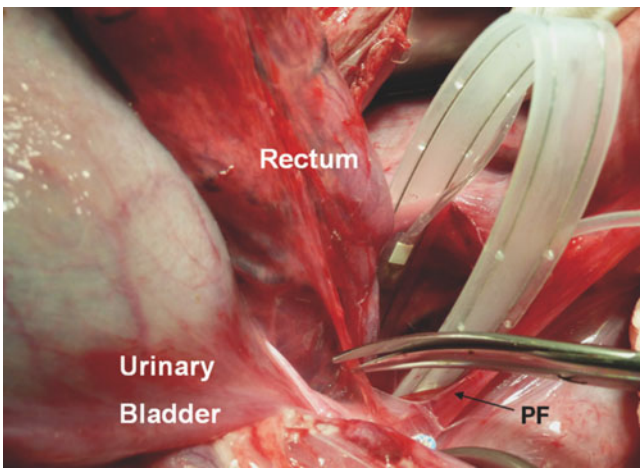

Fig. 3 Continuous monitoring of autonomic nerves on the left pelvic sidewall during left lateral rectal dissection. *PF* peritoneal fold

Replacement was successfully carried out after repeated intermittent neurostimulation. In all other animals, the tripolar electrode stayed in place during the whole operation. The median mesorectal dissection time was 10 min within a median number of ten (range 8–13) tripolar electric stimulations.

Continuous neuromonitoring resulted in sudden amplitude increases of the processed electromyographic signal of the internal anal sphincter, confirming intact autonomic innervation throughout the surgical procedure in each animal (median 0.9 μV interquartile range 0.5; 1.5 vs. median 3.4 μV interquartile range 2.1; 4.7) ($p<0.001$). All observed stimulation results, which have been intraoperatively assessed by the surgeon as positive responses, were evaluated as correct after additional postoperative data analysis.

The increased amplitude levels under continuous neuromonitoring on each pelvic side were in 41% (53 of 130) similar to the amplitude level of the first measurement (range ± 20%). Lower amplitudes were observed in 32% (42 of 130) and higher amplitudes in 27% (35 of 130). A comparison between the first amplitude increases and the following stimulation-induced amplitude levels demonstrated no significant difference for both pelvic sides in each animal ($p=0.317$). A complete signal loss during tripolar neurostimulation did not occur.

Final intermittent neurostimulation after low rectal resection confirmed bilateral intact innervation of the internal anal sphincter in each animal. The comparison of the median amplitude increases under intermittent neurostimulation after posterior mesorectal dissection and after low rectal resection demonstrated significantly decreased amplitude levels ($p=0.013$) (Fig. 4). At the end of the experiments, the pelvic autonomic nerves were injured by intentional

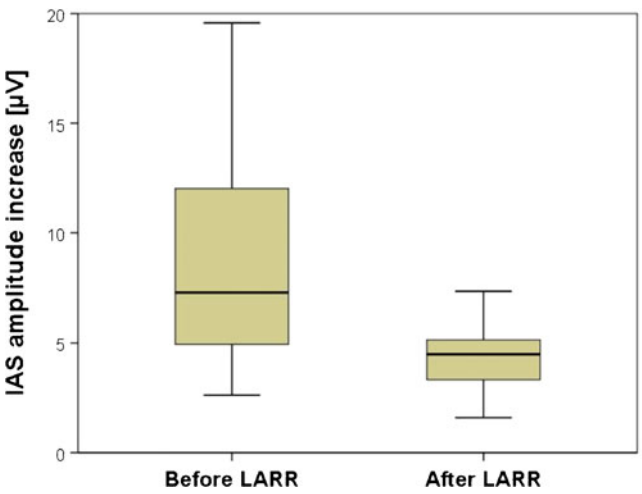

Fig. 4 Comparison of the intermittent stimulation results before and after low anterior rectal resection for all animals (Wilcoxon's signed rank test, $p=0.013$). *IAS* internal anal sphincter, *LARR* low anterior rectal resection

sharp severing distally to the stimulation sites at the level of the inferior hypogastric plexus. This resulted in absence of stimulation-induced increased amplitudes.

Discussion

The total mesorectal excision is a standardized surgical procedure and could be divided in posterior, lateral, and anterior dissection. Posterior rectal dissection is usually uncomplicated and injury to the superior hypogastric plexus and the hypogastric nerves can be avoided. Lateral and anterior dissection might be more challenging, especially if there is a narrow pelvis, thick mesorectum, additional bleeding, and a fixed low tumor causing difficulties in retaining the topographical overview. Straying out of the mesorectal plane in this area may result in injury to the inferior hypogastric plexus and its efferent fibers [17].

In the present experimental study, the median mesorectal dissection time was 10 min, which is quite short compared to the situation in humans. This could be explained by the intrapelvic neuroanatomy and topography of pigs, which is comparable to humans but less complex. For instance, in the investigated animals, only one ganglion on each pelvic sidewall could be observed, whereas efferences of the inferior hypogastric plexus in humans were conventionally described in the form of three up to five secondary plexus [18]. Furthermore, in pigs, the perirectal adipose tissue could not be traced around the extraperitoneal rectum. Loose connective tissue surrounding the rectum was found instead until the end of the anal canal [19]. Finally, the clinical situation is dealing with rectal cancer and could therefore not be compared to this experimental setup. However, this animal model offered the great possibility to perform a standardized procedure for the development of a methodological setup for continuous intraoperative neuromonitoring. This method facilitated the observation of functional nerve integrity during lateral and anterolateral dissection, where probably the autonomic nerves are at high risk for damage. This might be useful for precise determination of the mechanism and location of nerve injury or even serve as guidance during nerve-sparing surgery. For continuous neurostimulation, the pelvic splanchnic nerves were chosen as they are easier to identify and appear earlier than the inferior hypogastric plexus during the operation similar to our surgical procedure in the clinical practice. Moreover, a comparison of stimulation sites (pelvic splanchnic nerves vs. inferior hypogastric plexus) in a previous study demonstrated a trend towards higher amplitude levels of internal anal sphincter activity during stimulation of pelvic splanchnic nerves than among stimulation of the inferior hypogastric plexus [20]. The applied stimulation electrode for continuous neuromonitoring had a tripolar configuration, which reduced the occurrence of stray currents and permitted selective nerve stimulation. Implantation time is negligible, as no additional dissection of tissue or application of sutures is necessary. The electrode is self-stabilizing due to embedded rigid wires, forcing adhesion to the pelvic sidewall. Only one incidental electrode dislocation was observed in a stimulation-free interval, which could be attributed to the inappropriate size of the electrode, primarily developed for use in the human pelvis. Replacement of the dislocated electrode could be easily carried out. Overall, the tripolar surface electrode enabled simple and safe application. However, further technological developments are necessary and should be encouraged.

In all animals, stable and reliable induced electromyographic signals of the internal anal sphincter were recorded. Continuous neuromonitoring resulted in variable amplitude levels during lateral, anterolateral, and anterior mesorectal dissection. Schneider et al. pointed out that the quality of electromyographic signals depends on several factors, such as the used electrode, stimulation site, applied currents, surface contact of the electrode to the nervous tissue, and mechanical influences [21]. In the present study, a standardized procedure was performed with constant stimulation parameters. Increasing edema of the pelvic sidewall was observed during the operation, which might result in varying contact of the tripolar surface electrode to the nervous tissue. The application of a cuff electrode surrounding the nerve would increase signal quality [22] but needs surgical exposure. The dissection of this fine nervous tissue is nearly impossible and would result in unnecessary increased risk of nerve damage during electrode application. Therefore, a surface electrode as applied in this study is more favorable. Moreover, it is conceivable that manual rectal traction and compression and decompression of the pelvic sidewall, which were applied for proper dissection and maintenance of topographical overview, could also contribute to the variable amplitude levels. Nevertheless, signal loss during continuous neuromonitoring did not occur throughout the whole dissection in each animal, which indicated nerve-sparing and confirmed intact autonomic innervation. Initial clinical results in patients undergoing total mesorectal excision demonstrated that intermittent neuromonitoring of internal anal sphincter innervation is feasible [3]. Patients with positive stimulation results were fecal continent, whereas those with negative results demonstrated severed, impaired sphincter function at follow-up.

Interestingly, data of the present experimental study demonstrated significantly decreased amplitude levels after low rectal resection in comparison to the results after prior posterior mesorectal dissection. This might be due to rectal transsection, which incorporates severing of intramural (intrinsic) innervation of the internal anal sphincter. Direct injury to the sphincter could be excluded as resection was

performed at an adequate distance. However, it is conceivable that incidental partial autonomic nerve injury occurred by manual pulling of the rectum [23], which was necessary for low rectal myotomy. Whether the electromyographic amplitude level may provide information on the extent of nerve injury and consequently allows a prediction of the degree of postoperative dysfunction cannot be answered by the present study. Finally, reference values of amplitude levels and their changes during the dissection are needed. Therefore, clinical trials comparing the intraoperative stimulation results to the patients' functional outcome have to follow.

The severing of the autonomic nerves at the end of each experiment resulted in the absence of increasing amplitudes, which could be attributed to complete denervation of the internal anal sphincter. In the future, it is conceivable that such signal changes during total mesorectal dissection in a clinical setting may influence the intraoperative decision for a sphincter-saving procedure, assuming that the developed method reliably predicts postoperative anorectal function.

Conclusion

This experimental study demonstrated for the first time that continuous monitoring of autonomic nerves during low anterior rectal resection is feasible. The methodological setup provides sustained observation of autonomic neural pathways during critical parts of the mesorectal dissection, whereas intermittent neurostimulation provides information at selected points. The real-time feedback during dissection would be a new technical achievement, which may increase the surgeons' alertness with regard to autonomic nerve function and therefore limit nerve damage. It might also provide further insights into the pathophysiological mechanism of surgical nerve damage and objectifies critical areas and situations where nerve structures are at risk. Clinical application is not only limited to colorectal surgery but also to other specializations which perform nerve-sparing procedures in the small pelvis. For further investigations, a clinical trial in rectal cancer patients is being conducted.

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Conflicts of interest None.

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