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LETTER TO THE EDITOR

Urinary and sexual dysfunction after rectal cancer surgery: A surgical challenge

Theodoros Kolokotronis, Dimitrios Pantelis

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Abstract

This manuscript focused on the surgical challenge of urinary and sexual dysfunction after rectal cancer surgery based on the interesting results demonstrated by the observational study of Chen *et al*, which was published in the *World Journal of Gastrointestinal Surgery*. Urinary dysfunction occurs in one-third of patients treated for rectal cancer. Surgical nerve damage is the main cause of urinary dysfunction. Radiotherapy seems to exacerbate sexual dysfunction. The role of Denonvilliers' fascia preservation *vs* resection when performing total mesorectal excision (TME), the impact of robotic and transanal TME, alternatives to open and laparoscopic TME, as well as intraoperative pelvic neuromonitoring are discussed in this report. In conclusion, exact knowledge of the highly complex pelvic neuroanatomy and the use of novel surgical techniques can lead to a reduction in urinary and sexual dysfunction after rectal cancer surgery.

Key Words: Robotic total mesorectal excision; Intraoperative pelvic neuromonitoring; Sacral nerve stimulation; Denonvilliers' fascia

Core Tip: Urinary and sexual dysfunction have a significant negative impact on patient quality of life after rectal cancer surgery. New surgical techniques include robotic and transanal total mesorectal excision and intraoperative pelvic neuromonitoring. Knowledge of complex pelvic neuroanatomy, as well as the use of novel surgical techniques, can reduce the incidence of these complications.

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TO THE EDITOR

Colorectal cancer is the third most prevalent cancer in men (after lung and prostate cancer) and the second most common cancer in women after breast cancer[1]. Rectal cancer accounts for approximately 30% of all cases of colorectal carcinoma. The survival rates for patients with rectal cancer have significantly improved over time due to earlier diagnosis, the use of radiotherapy and the total mesorectal excision (TME)[2,3].

The TME technique, initially introduced by Heald[4] in 1979, relies on precise, sharp dissection under direct visualization, following natural, embryologically established planes. In this method the visceral fascia is separated around the mesorectum from the pelvic parietal fascia that covers the pelvic floor, rather than using blunt dissection[4]. TME is recognized as the gold standard for treating mid and low rectal cancer surgically. When combined with neoadjuvant radiotherapy, TME has shown a significantly lower local recurrence (< 5%) and a five-year survival rate of 80% for patients with mid and low rectal cancer[5,6]. Nonetheless, more than half of TME patients experience urogenital dysfunction, negatively impacting their quality of life (QoL)[7,8], with pelvic autonomic nerve damage being the primary cause of these postoperative complications[9]. Additionally, radiotherapy appears to worsen sexual dysfunction without affecting urinary function[10,11].

The multicenter Dutch TME trial provided long-term functional outcomes following rectal cancer surgery[3]. One thousand eight hundred and sixty-one patients with operable rectal cancer were recruited, who were randomly assigned to undergo TME with or without neoadjuvant radiotherapy. Patients completed questionnaires about urogenital functions preoperatively and postoperatively for up to five years period. Five years postoperatively, 38% of patients reported urinary incontinence with 72% of these individuals having normal function prior to surgery. Bladder emptying problems generally improved after 3 months, with 31% of patients experiencing a permanent dysfunction[12]. Among females, increases in general sexual dysfunction, dyspareunia and vaginal dryness were noted by 62%, 59% and 57%, respectively, while 76% of males reported general sexual dysfunction, with 80% experiencing erectile dysfunction and 72% reporting ejaculatory problems[3].

The symptoms of urinary dysfunction include urge to urinate, overflow or stress incontinence and retention[13]. Male sexual dysfunction includes erectile dysfunction (complete or partial) and ejaculatory problems. In women, lesion of sympathetic pathways results in impaired lubrication, vaginal dryness, decreased sensitivity of the internal genitalia and orgasm disorders. Conversely, damage to the parasympathetic pathways results in a weakened labial swelling response [13]. Therapeutic measures include sacral nerve stimulation for urogenital dysfunction and the prescription of phosphodiesterase-5 inhibitors for sexual dysfunction in males[14].

Impact of preservation vs Denonvilliers' fascia resection on urinogenital function

In a mini review published in the *World Journal of Gastrointestinal Surgery*, Chen *et al*[15] described the anatomy of Denonvilliers' fascia (DVF) and how relevant is during oncologic laparoscopic rectal resection. The DVF is a separate, thin layer of fascia that connects the rectum and its mesentery to the posterior wall of the seminal vesicle or prostate in males, and to the vagina in females. The DVF divides the anterior rectal space into two distinct fascial compartments: The anterior rectal space and the posterior prostatic space[16]. The Denonvilliers line serves as a critical anatomical landmark during TME, acting as a yellow-white boundary between the mesorectum and the pelvic fascia. The attachments of DVF in pelvic floor complicates dissection during surgical procedures, particularly in patients who have received neoadjuvant radiochemotherapy.

A randomized clinical trial by Fang *et al*[17] aimed to evaluate the advantages of DVF preservation compared to resection (NCT02435758). From August 26, 2015, to May 6, 2020, 262 male patients were enrolled and randomly assigned to either the laparoscopic TME (L-TME) with DVF preservation group (L-DVF-P) or the resection group (L-DVF-R) (n = 131 each). Six patients in the experimental group withdrew consent, and three had tumors found to be unresectable during surgery. In the control group, six patients withdrew consent and five suffered from unresectable tumors intraoperatively. These patients were excluded from the analysis. No significant differences were found between the two groups concerning age, body mass index, Eastern Cooperative Oncology Group performance status, American Society of Anesthesiologists physical status, and comorbidities, rates of neoadjuvant or postoperative adjuvant chemotherapy, or tumor characteristics[17].

Postoperatively, 40 patients (16.5%) died, with a median follow-up period of 51.9 months. The three-year overall survival (OS) rates were 94.1% for the experimental group and 89.7% for the control group (log-rank P = 0.22; HR, 0.56; 95%CI: 0.22-1.42). In the control group, the incidence of urinary dysfunction was 25.7% two weeks after surgery, significantly higher than the 6.3% reported in the experimental group. However, this incidence decreased over time, dropping to as low as 5.8% in the control group at three and six months post-operation. The rate of erectile dysfunction in the control group reached 39.0% at twelve months post-surgery[17]. Secondary outcomes, including three-year OS, three-year disease-free survival (DFS), and recurrence rates, were comparable between the groups. Overall, the findings suggest that L-DVF-P is associated with improved postoperative urogenital function while achieving comparable oncological outcomes for male rectal cancer patients[17].

Open vs laparoscopic vs robotassisted vs transanal TME in rectal cancer patients

In a recent review and meta-analysis, Geitenbeek *et al*[18] examined the functional outcomes related to urinary, sexual, and fecal functions, along with QoL, following various techniques for TME, including open surgery, L-TME, robot-assisted TME (R-TME), and transanal TME (TaTME). This analysis incorporated 19 studies that included 2495 patients, broken down into 88 who underwent open procedures, 1171 who received L-TME, 995 who had R-TME, and 241 who underwent TaTME. The quantitative comparisons between L-TME and R-TME indicated no significant differences in urinary or sexual function, with the exception of urinary function at three months post-surgery, in favor of R-TME[18]. The authors concluded that there were no significant differences in urinary, sexual, or fecal functions, nor in QoL across the different TME techniques. Previous systematic reviews and meta-analyses, however, have reported outcomes that are more favorable for R-TME and TaTME at six and twelve months follow-up compared to L-TME[19-22]. These differences may be due to the technical distinctions among the methods, with newer TME approaches potentially offering better visualization and a decreased likelihood of neurovascular lesions that can lead to urogenital dysfunction[18].

While innovative techniques such as R-TME and TaTME have shown to be oncologically safe, there remains a critical need for high quality, large-scale, multicenter prospective trials with adequate statistical power to evaluate functional outcomes and QoL. The authors emphasize that future research should take into account the learning curve and baseline patient characteristics, which will lead to a more comprehensive assessment of these vital aspects of rectal cancer surgery [18].

Given the current lack of long-term follow-up data regarding the influence of these advanced surgical techniques on patient QoL, there is keen interest in the results of international, multicenter, prospective cohort studies, such as the PROCaRe Study (NCT04936581), to provide clarity on this matter.

Role of intraoperative pelvic neuromonitoring during rectal surgery

Surgical injury to the pelvic nerves is a recognized cause of urinary, fecal, and sexual dysfunction following treatment for rectal cancer. Surgeons face the difficult task of accurately identifying and protecting the pelvic nerves during the layered dissection process. The use of pelvic neuromonitoring can significantly assist in locating the pelvic nerves, thereby helping to prevent postoperative autonomic nerve dysfunction[23-25].

The mechanism of nerve identification with intraoperative neuromonitoring involves directly stimulating the nerves within the surgical field and recording the corresponding responses from the target organs through electrophysiological methods. Developing intraoperative neuromonitoring techniques specifically for autonomic nerves is challenging because established methods, such as electromyography (EMG) and the recording of evoked potentials, primarily apply to motor and sensory nerves, which exhibit different responses to stimulation compared to autonomic nerves[26].

The only existing pelvic neuromonitoring technique has been explored by research group of Kauff and Kneist, focusing on direct stimulation of the pelvic nerves during surgery, as well as EMG measurements of the internal anal sphincter (IAS) and bladder manometry. This EMG method helps to detect autonomic biosignals intraoperatively. An increase in EMG activity of the IAS during direct nerve stimulation is interpreted as a positive signal response[25,27].

The NEUROS trial investigated whether pelvic intraoperative neuromonitoring (pIONM) could improve functional outcomes related to urogenital and ano-(neo-)rectal function in patients undergoing TME for rectal cancer. This trial was a two-arm, randomized, controlled, multicenter study involving 189 patients who had TME performed across eight different centers from February 2013 to January 2017. The procedures were conducted with pIONM (n = 90) or without it (control group, n = 99).

Logistic regression analysis showed favorable results for the pIONM group (OR: 0.342; 95%CI: 0.124-0.944; P = 0.038). No significant differences could be found in relation to patient sex, neoadjuvant therapy, or the baseline International Prostate Symptom Score[25].

Moreover, at the twelve-month follow-up, the pIONM group had significantly higher mean scores on the International Index of Erectile Function than the control group[25].

The NEUROS prospective randomized multicenter trial found that a significantly smaller percentage of patients who underwent TME with pIONM experienced considerable deterioration in urinary function one year post-surgery compared to those without this method (8% *vs* 19%), highlighting the importance of intraoperative pIONM in preventing pelvic autonomic dysfunction[25].

Additionally, a prospective trial published in Nature Scientific Reports by Ramona Schuler and colleagues demonstrated the feasibility of a novel method for intraoperative pelvic neuromonitoring based on bioimpedance measurements during robotic rectal surgery[26]. In this clinical investigation (German Clinical Trials Register DRKS00017437, first registered on March 31, 2020), thirty patients (16 males and 14 females) underwent nerve-sparing rectal surgery using a new approach that combined direct nerve stimulation with impedance measurements of target organs. The technical success was confirmed in 93.3%, though further investigation into long-term patient outcomes and additional evidence supporting this technique's effectiveness are still needed[26].

CONCLUSION

A good understanding of the pelvic anatomy, as well as the use of novel surgical techniques (R-TME and Ta-TME) and instruments (intraoperative pelvic neuromonitoring), can contribute to a significant reduction in urogenital dysfunction after rectal cancer surgery, although more evidence is needed to further evaluate the long-term outcomes of novel surgical techniques.

FOOTNOTES

Author contributions: Kolokotronis T conceived the design of the experiment, analyzed the data and wrote the manuscript; Pantelis D critically revised the manuscript.

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