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Neurogenic bladder dysfunction after total mesorectumectomy

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ABSTRACT *AIM: to estimate the rate, causes and features of neurogenic bladder dysfunction in patients with rectal cancer after total mesorectumectomy.*

PATIENTS AND METHODS: the results of surgical treatment of 103 patients with rectal cancer were analyzed in the light of immediate and long-term outcomes, who underwent total mesorectumectomy using traditional (56-54.4%) and laparoscopic (47-45.6%) technologies. In 20 (19.4%) of 103 patients, the course of the immediate postoperative period was complicated by the development of neurogenic bladder dysfunction. In order to study the frequency of neurogenic bladder dysfunction depending on the technique of mesorectumectomy, the patients were divided into 2 groups. Group 1 included 9 patients who underwent laparoscopic total mesorectumectomy. Group 2 included 11 patients who underwent traditional (open) mesorectumectomy.

RESULTS: the study of the functional state of the bladder according to the flowmetric indicators revealed that the frequency of development of postoperative bladder dysfunction has a gender dependence. The frequency of neurogenic bladder dysfunction was 25% in men and 10.7% in women. It is shown that during 1 week and 6 months after surgery, the average urination rate tends to increase in women and decrease in men, regardless of the technique of total mesorectumectomy. In both groups, there was not a statistically significant decrease in the maximum volumetric velocity in both men and women within 6 months after surgery. At the same time, during this period, there was a decrease in the average rate of urination only in men, regardless of the technique of total mesorectumectomy. And in women, this indicator remained unchanged or slightly increased.

CONCLUSION: it is shown that a complex system of therapeutic measures, including drug stimulation of the detrusor and urethral sphincter, repeated catheterization of the bladder, as well as epicystostomy performed according to indications, allows adequate correction of bladder dysfunction after total mesorectumectomy in patients with rectal cancer.

KEYWORDS: rectal cancer, total mesorectumectomy, open total mesorectumectomy, laparoscopic total mesorectumectomy, neurogenic bladder dysfunction

CONFLICT OF INTEREST: The authors declare no conflict of interest

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INTRODUCTION

Global trends in the epidemiology of colorectal cancer (CRC) clearly demonstrate the high incidence of rectal cancer (RC), which consistently occupies the 4–5th place in the overall structure of malignant tumors [1–4]. According to our data, after total mesorectumectomy (TME) performed using traditional (open) TME (OTME), the actual survival rate was 81.8%, the disease-free

3-year survival rate was 60.6%. In patients who underwent TME using laparoscopic technology (LTME), these indicators were 80% and 56.7%, respectively. After OTME, the 5-year actual survival rate was 54.5%, the disease-free 5-year survival rate was 31.8%. In patients who underwent LTME, these data were 57.8% and 31.6%, respectively [5].

The presented data demonstrating the level of morbidity and mortality convincingly indicate

the global medical and social significance of the problem of CRC in general, and RC in particular. Since the 80th year of the twentieth century, the transition from the standard, so-called “orthodox” surgery for RC to the TME technique, developed by Heald, R.J. et al. [7], and providing for the removal of the rectum in a single block together with anatomical structures located within its fascial “case” with the preservation of elements of the autonomic nervous system of the pelvis (ANSP), marked the beginning of a new era in oncoproctology and opened a new direction in the surgical treatment of RC. However, many authors [1,6] regret to note that, despite the obvious advantages, it has not yet been possible to achieve the widespread introduction of the TME technique as a standard surgery for RC.

Meanwhile, being a functionally sparing and sphincter-preserving surgery, TME meets all the principles of oncological radicality and makes it possible to improve not only long-term outcomes, but also the early functional results of surgical treatment of RC. As a nerve-sparing surgery, TME allows to ensure the safety of the visceral fascia of the rectum and the integrity of the autonomous (autonomic) nervous system of the pelvis (ANSP) and thus does not lead to a significant violation of the function of the lower urinary system and a decrease in the quality of life in operated patients [8]. According to Sidorov, D.V. et al. [6], the use of the nerve-sparing technique during TME makes it possible to significantly reduce the incidence of urological complications and restore bladder function in 90.3% of patients in the early postoperative period. However, despite the undeniable advantages, TME is not without drawbacks, which include urological complications, sexual disorders, anal incontinence. This is due to the fact that rectal surgeries in general, TME — in particular, belong to the category of technically complex, traumatic procedures with a high risk of complications and mortality.

To denote the disorder of the function of the lower urinary system in patients with RC after TME, many similar terms are used in the literature: “urodynamic disorders”, “urological complications”, “detrusor dysfunction”, “neurogenic

bladder dysfunction”, etc. It seems to us that using different terms reflecting different linguistic interpretations, the authors put a single semantic meaning into them.

Regarding the causes of neurogenic bladder dysfunction (NBD) after TME, there are different opinions among surgeons. Many authors [9–12] believe that the development of this complication is directly caused by intraoperative damage to the elements of the ANSP associated with insufficient visualization of the surgical field during surgery. According to other authors [13,14], an important role in the development of NBD is played by the local spread of the tumor with involvement in the malignant process of ANSP, requiring the removal of affected adjacent tissue structures. The frequency of locally advanced RC with involvement of the visceral fascia of the rectum and invasion of the tumor into adjacent organs and anatomical structures of the pelvis, is 26–35% [15,16]. At the same time, in 50.3–60.2% of cases, the lesion falls on the urinary system involvement [17,18]. After TME, bladder dysfunction occurred in 9–40%, according to some authors [27,30] from 9% to 40%. Other authors revealed it in 48–80% [20,21].

The high percentage of NBD is due to the close anatomical and topographic relationship of the pelvic organs on the one hand and the involvement of neighboring organs and anatomical structures of the pelvis in the tumor process on the other hand. And finally, an important role in the structure of the causes of the development of this complication is played by the traumatic nature of surgeries performed in patients with locally advanced RC, as well as neoadjuvant chemoradiotherapy performed in the preoperative period. According to the literature [22–24], 5.2–17.6% of patients develop persistent bladder atony after neoadjuvant chemoradiotherapy. The development of NBD significantly aggravates the course of the postoperative period and worsens the quality of life of patients. Chronic bladder dysfunction contributes to a violation of the passage of urine with the possible development of hydronephrosis and, as a consequence, chronic renal failure [6].

In recent years, publications have appeared in the literature demonstrating the effectiveness

Table 1. Neurogenic bladder dysfunction in patients with rectal cancer, depending on gender and TME technique

TME Technique	Total	Males	Females	Total
LTME	27	6 (22.2%)	3 (11.1%)	9 (33.3%)
OTME	29	8 (27.6%)	3 (10.3%)	11 (38%)
Total	56	14 (25%)	6 (10.7%)	20 (35.7%)

Note: The table does not include 36 patients (18 patients from each group), in whom independent urination was restored after the first catheter removal.

of the intraoperative neuromonitoring method in order to identify and preserve the integrity of the elements of the ANSP [25–27]. However, the authors declare that as an intraoperative method for determining the ANSP, this method currently can hardly be qualified as the main one, but it has prospects from the point of view of studying the physiology of the pelvis. According to the cited authors, further accumulation of experience in the use of the intraoperative neuromonitoring method will allow determining its significance in RC surgery.

Thus, the presented literature data allow us to state that the study of the causes, frequency and features of NBD in patients with RC after TME has important scientific and practical significance, and the search for rational surgical methods that ensure compliance with the principles of anatomical zonality and oncological radicalism seems very relevant.

AIM

To assess causes and features of the clinical picture of NBD in patients with RC after TME.

PATIENTS AND METHODS

The retrospective study is based on the results of checkup and surgical treatment of 103 patients aged 20 to 70 years with cancer of the middle and lower ampullary segments of the rectum. The diagnostic algorithm included general clinical, laboratory, biochemical and instrumental methods of diagnostics (thorax X-ray,

transabdominal, endorectal and transvaginal ultrasound, colonoscopy, CT of the thorax and abdominal cavity, MRI of the pelvic organs, electrocardiography, echocardiography). The diagnosis was verified also by cancer markers (CEA and CA-19-9) and pathomorphology of biopsy and removed specimen. To assess the functional state of the urinary system, uroflowmetry was performed.

All patients under endotracheal anesthesia underwent total mesorectumectomy, using traditional (open) technology in 56 (54.4%), laparoscopic — in 47 (45.6%) cases. Particular attention was paid to the macroscopic examination of the removed specimen in order to visually assess the preservation of the visceral fascia, the degree of severity and integrity of mesorectum, the presence or absence of intraoperative perforation of the intestinal wall. In all patients, the histological structure of the tumor was represented by adenocarcinoma of various degrees of differentiation. In the early postoperative period, bladder dysfunction occurred in 56 (54.4%) of 103 patients. There were 31 men (55.4%) and 25 women (44.6%). All patients had locally advanced RC ($T_{3-4}N_{1-2}M_0$).

All patients underwent neoadjuvant chemoradiotherapy in the preoperative period. Analysis of the causes of NBD shows that these complications were caused either by tumor lesions (in 29 cases) or intraoperative lesions (in 27 cases) of the visceral nerves during surgery. In 27 (48.2%) of 56 patients, TME was performed using laparoscopic technology (Group 1), in 29 (51.8%) — traditional (Group 2) (Table 1).

All patients underwent procedures without nerve-sparing technique. Assessment of the degree of preservation of the visceral nerves was

carried out visually. In the group of patients who underwent LTME, urodynamic disorders developed as a result of iatrogenic damage to the visceral nerves in 15, tumor lesion — in 12 cases. Of the 29 patients who underwent OTME, the occurrence of urodynamic disorders was due to intraoperative damage to the ANSP in 12, tumor lesions in 17 cases. It should be noted that intraoperative damage to the visceral nerves was due to technical difficulties in performing certain stages of TME associated with anatomical and topographic features of the location of organs and the complexity of intraoperative identification of the nerve trunks of the pelvis. The manifestation of the “NBD” syndrome was characterized by acute urinary retention, an increase in the volume of residual urine, and a weakening of the feeling of filling the bladder. This symptom complex was evaluated taking into account the complaints of patients, characteristic clinical manifestations, the results of physical examination and ultrasound examination of the pelvic organs. In order to objectively assess the contractility of detrusor, all patients underwent daily registration of the state of urination by uroflowmetric monitoring. Uroflowmetry was performed using a portable device — uroflowmeter, model “AGAT” (Russia). The uroflowgram based on the registration of urination parameters was evaluated according to the following indicators: — urination time (normally < 10 sec); — maximum volume urination rate (normally > 15–20 ml per second); — average urination rate (normally > 10 ml per second); — time to reach maximum speed; — total volume of urination (more than 50 ml); — waiting time for the start of urination (normally < 10 seconds).

Of these parameters, the maximum volumetric velocity and average urination rate were considered practically significant.

Statistical processing of the results of the study was carried out on a personal computer using software tools and the SPSS for Windows 13.0 package. The significance of the differences was assessed using the nonparametric Wilcoxon-Mann-Whitney method for independent samples. The differences were considered statistically significant at $p < 0.05$.

RESULTS

After the first catheter removal, self-urination was restored in 9 (60.0%) men and 9 (75.0%) women who underwent LTME. Self-urination after the first catheter removal was restored in 10 (77.0%) women and 8 (50.0%) men who underwent OTME. As can be seen from the presented data, after the first catheter removal, the restoration of self-urination was equally often observed both in patients who underwent LTME and in patients who underwent OTME. For the first 3 days of the postoperative period, it was not possible to restore independent urination in 9 patients who underwent LTME (6 men, 3 women). A similar pattern was observed in 11 patients (8 men, 3 women) after OTME. In 18 patients (in 8 — after LTME, in 10 — after OTME), urine removal was carried out by repeated catheterization of the bladder and the installation of a permanent catheter. The age of the patients in the study group ranged from 53 to 70 years. In the middle age group (44–66 years) there were 7 (35.0%) patients, in the elderly (60–70 years) — 13 (65.0%). There were 14 men (70.0%), 6 women (30.0%).

For the purpose of drug correction of NBD, all the patients were prescribed a cholinomimetic drug — 0.05% solution of neostigmine (proserin). The drug was administered intramuscularly 1 ml 3 times a day for a week.

To stimulate the contractile function of detrusor in men, omnik (tamsulosin, a drug from the group of α_1 -blockers) was prescribed 1 capsule per day for 2 weeks. Independent urination by the time of discharge from the hospital was restored in all these patients. Urine derivation was performed by trocar epicystostomy in two patients aged over 60 years who underwent LTME (1) and OTME (1) and suffered from benign prostatic hyperplasia. Restoration of self-urination in these patients occurred within 6 months after TME. No cases of “catheter-associated” urinary tract infection were detected. A comparative assessment of the degree of postoperative NBD according to the parameters of uroflowmetry, taking into account the patients’ gender, revealed that within 1 week and 6 months after surgery, the average urination rate (AUR) tends

Table 2. Dynamics of the maximum volume and average urination rate according to uroflowmetry data at different times after TME in patients with rectal cancer

	LTME				OTME			
Gender	MVRU		AUR		MVRU		AUR	
	1 week	6 months	1 week	6 months	1 week	6 months	1 week	6 months
Males	20.8 ± 2.1	20.6 ± 4.2	16.2 ± 2.5	16.2 ± 3.2	20.1 ± 1.9	20.5 ± 4.1	16.3 ± 2.4	16.3 ± 3.4
Females	20.1 ± 1.0	18.1 ± 3.9	17.4 ± 1.6	17.8 ± 3.5	20.2 ± 1.1	17.9 ± 3.7	17.5 ± 1.7	17.9 ± 3.6

Note: The table does not include 36 patients (18 patients from each group), in whom independent urination was restored after the first catheter removal.

to decrease in men, regardless of the TME technique. In both groups, there was a significant decrease in the maximum volumetric rate of urination (MVRU) in both men and women within 6 months after surgery. At the same time, for this period, there was a decrease in AUR only in men, regardless of the TME technique. And in women, this indicator remained unchanged or slightly increased. The changes of MVRU and AUR according to uroflowmetry data at various times after TME is presented in Table 2.

Thus, the analysis of our clinical cases shows that NBD after TME in patients with RC is almost equally common in patients who have undergone both LTME (in 33.3%) and OTME (in 38%). The occurrence and clinical picture of NBD have a gender feature, regardless of the TME technique. Thus, the incidence of NBD in men was 25%, which is over 2 times more than the same indicator in women — 10.7% (Table 1).

DISCUSSION

The relevance of the RC problem is due not only to the complexity of solving oncological problems associated with ensuring long-term actual and disease-free cancer survival, but also to the difficulty of improving the immediate functional results of surgical treatment. One of the unresolved problems of RC surgery is NBD, which develops in the early postoperative period [9–14]. The complexity of topographic anatomical relationships of the pelvic organs create prerequisites and potential threats to damage

the visceral nerves, innervating organs of the genitourinary system. In addition to intraoperative damage to the visceral nerves, with RC, the spread of the malignant process through the perineural spaces is possible, which is also an unfavorable prognostic sign in relation to both immediate functional and long-term oncological results of surgical treatment [6,17–20]. On the other hand, reliable methods for determining the degree of tumor invasion into the visceral nerves and intraoperative identification of the nerve structures of the pelvis have not yet been developed [6]. Meanwhile, the report of individual authors [25–27] on the effectiveness of the intraoperative neuromonitoring method in order to identify and preserve the integrity of the visceral nerves, inspires some optimism about improving the functional results of surgical treatment of patients with RC.

The introduction of functional-sparing surgeries into the arsenal of surgical treatment of patients with RC allows to preserve the integrity of the ANSP elements as much as possible and reduce the frequency of bladder dysfunction. The frequency of NBD after TME in patients with RC varies widely, varying from 40% to 80% [16,19–21]. According to our data, the total proportion of NBD in patients with RC was 35.7%, which developed both after OTME (in 38%) and after LTME (in 33.3%).

Treatment and rehabilitation of patients with NBD after TME is a difficult and complex task. Unfavorable is the fact that to date there is no generally accepted concept of treatment of NBD in patients with RC after TME in the literature.

The principles of correction of postoperative disorders of bladder function include a multicomponent system of therapeutic measures taking into account the clinical manifestation of NBD in accordance with uroflowmetric parameters. One of the important criteria for objectively assessing the functional state of the bladder is the restoration of self-urination after the first catheter removal. Sidorov, D.V. et al. [6] revealed recovery of spontaneous urination after the first catheter removal in 90.3% of the operated patients. According to the authors, in 9.7% of cases in the early postoperative period (for no more than 3 days), it was not possible to restore independent urination, which required repeated catheterization of the bladder. In our study, in the absence of restoration of self-urination, 18 (90.0%) of 20 patients underwent repeated catheterization of the bladder with the installation of a permanent catheter. Two (10.0%) patients aged over 60 years, suffering from benign prostatic hyperplasia had urine excretion performed by trocar epicycstostomy. Independent urination in all these patients was restored within 6 months after surgery. The effectiveness of prolonged catheterization with persistent bladder atony in patients after TME is confirmed by the works of other authors [19,28]. Along with routine methods (permanent catheterization of the bladder, drug stimulation of detrusor, etc.), some authors [29] consider

advisable the use of α_1 (alpha₁)-adrenoblockers (tamsulosin, terazosin, alfuzosin, silodosin), among which tamsulosin and silodosin have the greatest uroselectivity, for the purpose of pharmacological correction of NBD in men. It is also recommended to use α_1 -adrenoblockers combined with phosphodiesterase inhibitors of type 5 (PDE-5) (sildenafil, vardenafil, tadalafil, etc.) in men whose NBD is accompanied by sexual dysfunction.

AUTHORS CONTRIBUTION

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