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COMPARATIVE ANALYSIS OF CIRCUMFERENTIAL RESECTION MARGIN CONDITION DURING THE LAPAROSCOPIC AND OPEN TOTAL MESORECTAL EXCISION

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The research work was carried out under the examination and treatment of 103 patients diagnosed with rectal carcinoma. The patients were divided into 2 semi-groups: 47 patients implemented total mesorectal excision in a laparoscopic way; 56 patients implemented total mesorectal excision in an open way. MRT examination of the small pelvis, CT examination of the chest cavity and abdominal cavity, colonoscopy, appointment of the oncomarkers in blood and other methods of examination were used in the course of the research. The factors like the tumor size, invasion depth, metastatic damage of the mesorectal lymph nodes, tumor emboles, tumor deposits, distance from the anus, phase of the tumor process and quality of the total mesorectal excision have statistical exact effect on the circumferential resection margin status during the pathohistological examination of the drug made. The circumferential resection margin was positive in T_3/T_4 masses in 66.7 % cases, in the patients with their lymph nodes damaged metastatically in 57.1 % cases, in the tumors of III phase in 57.1 % cases, in large tumors more than 4cm in 50 % cases. 33.3 % local recurrence was noted in these patients ($p<0.05$).

Key words: Rectal carcinoma, circumferential resection margin, total mesorectal excision, tumor embolus, tumor deposits, metastatic lymph nodes.

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ПОРІВНЯЛЬНИЙ АНАЛІЗ СТАНУ КРАЮ КРУГОВОЇ РЕЗЕКЦІЇ ПРИ ЛАПАРАСКОПІЧНІЙ І ВІДКРИТІЙ ТОТАЛЬНІЙ МЕЗОРЕКТАЛЬНІЙ ЕКСЦИЗІЇ

Дослідницька робота проводилася при обстеженні та лікуванні 103 хворих з діагнозом рак прямої кишки. Пацієнти були розділені на 2 напівгрупи: 47 хворим виконано тотальну мезоректальну ексцизію лапароскопічним шляхом. Тотальне мезоректальне висічення відкритим способом виконано 56 хворим. У ході дослідження застосовували МРТ малого тазу, КТ органів грудної та черевної порожнини, колоноскопію, визначення онкомаркерів у крові та інші методи дослідження. Такі фактори, як розмір пухлини, глибина інвазії, метастатична ураження мезоректальних лімфатичних вузлів, пухлинні емболи, пухлинні відкладення, відстань від ануса, фаза пухлинного процесу та якість тотальної мезоректальної ексцизії надають статистично точний вплив на статус циркулярного краю резекції при патогістологічному дослідженні, проведено експертизу препарату. Циркулярний край резекції був позитивним при утвореннях Т3/Т4 у 66,7 % випадків, у хворих з метастатичним ураженням лімфатичних вузлів у 57,1 % випадків, при пухлинах III фази у 57,1 % випадків, при великих пухлинах понад 4см у 50 % випадків. У цих хворих відмічено 33,3 % місцевих рецидивів ($p<0,05$).

Ключові слова: рак прямої кишки, циркулярний край резекції, тотальна мезоректальна ексцизія, пухлинні емболи, пухлинні депозити, метастатичні лімфатичні вузли.

The solution to the problems that appeared during the treatment of rectal carcinoma was always at the center of attention of the local and foreign coloproctologists. The illness with rectal carcinoma ranges between 9.0 % and 19 % in the developed counties among the malignant masses. The illness with rectal carcinoma made up 18 people per 100 thousand people by 800 thousand people all over the world every year. The illness with rectal carcinoma changes on large scale all over the world. If it is connected with different diets, alcohol, cigarette, obesity, and less physical activeness, on one hand, the role of hereditary factors is unavoidable on the other hand [3, 9].

The illness with rectal carcinoma ranged between the ages of 59 and 62 on average in Turkmenistan, Kyrgyzstan as well as in Azerbaijan. A multidisciplinary approach is preferred in the treatment of rectal carcinoma in modern times. If radiation chemotherapy is preferred in the treatment of rectal carcinoma in Brazil, multidisciplinary treatment (radiation therapy, surgical treatment, post-operational chemotherapy if necessary) is preferred in the United States of America and some other countries, as well as us [8, 10]. Carrying out short and long (Swedish protocol) radiation therapy before the operation depending on the phase of carcinoma is nearly accepted all over the world. The total mesorectal excision (TME) to be performed in the patients who received this course of treatment, is received as a gold standard in the treatment of rectal carcinoma [2, 4].

Removal of the fat tissue and mesorectal fascia covering it together with the tumor covering the rectum as a whole is called total mesorectal excision. The TME performed without violating the integrity

of the mesorectal fascia is assessed as high quality TME (Grade 3) but the TME implemented with the damage of this fascia acutely, as low-quality TME (Grade 1). The distance between the tumor, the deposits and emboles of tumor and mesorectal fascia (circular resection border, CRM) must certainly be taken into account while assessing the quality of TME [11, 12]. If the CRM status is 1mm<, despite of the high quality of TME, the probability of local recurrence increases from 5.8 % to 16 %, the ability of giving of long metastasis from 12.7 % to 37.6 %. Therefore, the assessment of the CRM status with the methods of examination (MRT) is of exceptional importance. The role of radiotherapy conducted before operation with the only way of directing of the CRM status to negative (CRM 1mm>) in the patients with positive CRM status (CRM 1mm<) has already been proved with multiple research works [5, 6].

The purpose of the study was a comparative study the factors (direct development of tumor, tumor deposits, tumor embolus, lymph nodes) affecting the CRM during the total mesorectal excision by laparoscopic and open way of surgery.

Materials and methods: The research work was carried out under the examination and treatment of 103 patients diagnosed with rectal carcinoma at the Clinical Medical Center, which is the base of the Surgical Diseases Department I of Azerbaijan Medical University and the private clinic "Elmed" Medical Center in 2010–2015. The patients were divided into 2 semi-groups: 1) 47 patients implemented total mesorectal excision in a laparoscopic way (LTME); 2) 56 patients implemented total mesorectal excision in an open way (OTME). The distribution of the patients according to their age and sex is mentioned in the Table 1.

Table 1

Distribution of patients by age and gender

Age	LTME (n=47)				OTME (n=56)			
	Male (n=20)		Female (n=27)		Male (n=26)		Female (n=30)	
	Abs.	%	Abs.	%	Abs.	%	Abs.	%
20–29	1	5.0	–	–	–	–	1	3.3
30–39	2	10.0	1	3.7	1	3.8	2	6.7
40–49	4	20.0	5	18.5	2	7.7	6	20.0
50–59	5	25.0	7	25.9	7	26.9	9	300
60–69	7	35.0	11	40.7	13	50.0	10	33.3
70>	1	5.0	3	11.1	3	11.5	2	6.7
Total	20	100	27	100	26	100	30	100
p	$\chi2$=4.426 p=0.490		$\chi2$=1.769 p=0.880					
pU	$\chi2$=1.014 p=0.961							

We divided the rectum into 3 regions as inferior rectum (0–6 cm), average rectum (7–12 cm) and superior rectum (12 cm>) anatomically. The localization of the masses was also conducted according to this division (Table 2).

Table 2

Localization of rectal malignancies relative to the distance to the anal canal

Distance from the anus	LTME (n=47)		OTME (n=56)	
	M	%	M	%
0–6 cm	13	27.7	16	28.6
7–12 cm	18	38.3	22	39.3
>12 cm	16	34.0	18	32.1
$\chi2$; p	$\chi2$=0.042; p = 0.979			

The distribution of the patients in the LTME and OTME groups was as follows depending on the depth of invasion of the rectal cysts: 5 patients in T_1 phase, 21 patients in T_2 phase, 65 patients in T_3 phase and 12 patients in T_4 phase. The distribution of the patients over the phases (over both groups) according to TNM classification systems with the phases: I phase – $T_{1\text{-}2}N_0M_0$, II phase $T_{3\text{-}4}N_0M_0$, III phase $T_{1\text{-}4}N_{1\text{-}2}M_0$ are following: I – 14.9 % in LTME and 8.9 % in OTME; II – 25.5 % and 28.6 %; III – 59.6 % and 62.5 %, respectively ($\chi2$ = 0.903; p = 0.637). The patients of long metastasis (M1) were not included in the research.

We considered it advisable for classifying the patients in T_3 and T_4 phases in a separate subgroup along with dividing them into classic phases. The depth of spreading of the cyst tissue in mesorectum were classified as following: pT_{3a} – up to 1 mm, pT_{3b} 1–5 mm, pT_{3c} 5–15 mm, pT_{3d} 15 mm>, Pt_{4a} (i.) – invasion applicable to the adjacent organs (i.), Pt_{4b} (n.i.) – invasion not applicable to the adjacent organs (n.i.). Thus, in LTME group percentage of patients with pT_{3a} was 18.2 %, in OTME group – 16.7 %; with pT_{3b} – 18.2 % and 19.1 %, respectively; pT_{3c} – 24.2 % and 26.3 %, respectively; pT_{3d} – 27.3 % and 23.8 % respectively; pT_a – 3.0 % and 7.2 %, respectively; Pt_{4b} – 9.1 % and 11.9 %, respectively.

There was disclosed adenocarcinoma of different differentiation in most cases during the pathohistological examination of the surgical materials removed. The MRT examination of small pelvis, CT examinations of the chest cavity and abdominal cavity, colonoscopy, appointment of the oncomarkers in blood and other methods of examination were used in the course of the research.

The calculations were processed in the statistical package SPSS-26 using the criteria of variational (U-Mann-Whitney (pU): H.-Kruskal-Wallis), discriminant (χ^2-Pearson) and variance (F-Fischer) analysis.Comparison between groups were done with an analysis of variance (ANOVA). A statistical difference was determined by a value of $p<0.05$.

Results of the study and their discussion. The distance between the tumor elements and mesorectal fascia is called as circular resection border. This distance may be measured by investigating the MRT results before the operation and assessed under the pathohistological examination of the material removed after the operation. Being of the CRM 22 mm bigger is assessed as the negative CRM but being of it 22 mm smaller as the positive CRM. The above-mentioned distance is of unbelievable importance with respect to the recidivation of the tumor. If the CRM+ (positive), then the probability of occurrence of local recurrences is 62.5 % (75) during the TME conducted. If the CRM is assessed as positive before an operation, this time, it is not possible to fully treat the disease only by conducting a surgical operation. The radiochemotherapy course conducted before an operation, is an only method of treatment that could make the CRM as negative. Long (short) radiochemotherapy course leads to increasing of surgical clearance by destroying the tumor elements which make the CRM as positive that as a result, both the quality of the TME increases and the probability of giving of local recurrence minimizes. In cases the CRM is assessed before the operation (in the radioresistant masses), the CRM may be disclosed to be positive during the pathohistological examination of the material removed after the operation. In such cases, it should not be forgotten that it may happen with local recurrence and the patient should be notified. The probability of the CRM to be positive in T_1 and T_2 masses in I phase (the tumor has not gone out of the wall of the intestine) during the investigation of the effect of the invasion depth of the tumor on the CRM. In such cases, the occurrence of local recurrence is connected with serious technical errors during the conduction of the TME. The probability of positivity of the CRM also increases together with spreading of tumor in the mesorectal tissues in T_3, especially in T_4 masses and invasion of it to the serous membrane ($\chi 2=26.662$; $p<0.001$). (Figure 1).

The results mentioned in the Figure 1, are provided according to the MRT examinations conducted before the operation. The reason for being of positive of the CRM in 1 patient of T_1/T_2 group is connected with locating of the mass in T_2 phase in the inferior anterior region of the rectum. The lack of mesorectal tissue here leads to being of the distance between the mass and (T_2) mesorectal fascia less than 2 mm, that is, the positivity of the CRM.

The radiochemotherapy course conducted before the operation has its positive effect on the CRM status. It is possible to obtain positive dynamism in about 60–70 % cases on the account of sucking of the tumor elements affecting the CRM status on the account of the radiotherapy treatment conducted in the region of tumor. There happens both the reduction of the sizes of the tumor itself and the suction of the embolus and lymph nodes on the account of the treatment conducted. The CRM was negative in 14 (63.6 %) patients, positive in 8 patients (36.4 %) in the LTME group but positive in 8 patients (30.7 %) and negative in 18 patients (69.3 %) in the ATME group during the MRT re-examination after the radiotherapy course conducted in the patients (22 and 26 patients correspondingly) of the LTME and OTME groups with positive CRM before the operation.

Our observations show that statistical exact difference does not exist among the groups with respect to the CRM status. But differences of statistical importance exist between T_1/T_2 group and T_3/T_4 group. And it shows how the invasion degree of the tumor is important in respect of the CRM status. Being of positive of the CRM even after the radiotherapy course conducted in the patients with positive CRM, increases the probability of local recurrence after the surgical intervention to be conducted in the LTME and OTME groups (36.4 % and 30.7 %) accordingly. But as there is not anything left to do in this kind of conditions, it is necessary to make surgical intervention and wait for the local recurrences to happen as well as give information to the patient (close people of the patient) about it.

As the other factor that can affect the CRM is lymph node, it assumes special interest to study the effect of this kind of metastases on the CRM status. The existence of metastases in the regional lymph nodes shows the spreading of the tumor process that it has an effect on the quality of the surgical intervention (TME). The metastases in the mesorectal lymph nodes in the monitoring groups are met in 61.1 % cases over both groups ($\chi 2=5.957$; $p = 0.015$). It is mentioned in the Figure 2.

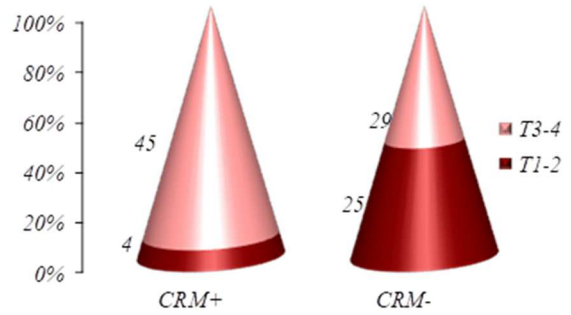

Figure 1. Effect of the invasion depth on the circular resection border.

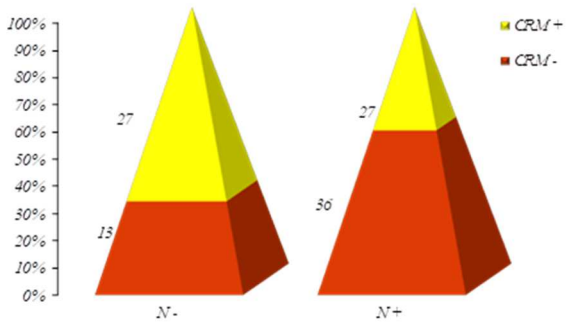

Figure 2. Effect of metastatic damage to mesorectal lymph nodes on the CRM in both groups.

There is not any difference among the LTME and OTME groups with respect to the positivity of the CRM. But statistical exact differences exist among N- and N+ within the group with respect to the positivity of the CRM. The CRM was positive in 57.1 % (LTME and OTME) during the metastatic damage of the lymph nodes over both groups correspondingly. The positivity of the CRM became 15.7 % and 14.2 % in the patients with intact (or hyperplastic) lymph bodes without metastasis in the LTME and OTME groups accordingly. All of the patients with positive CRM, were the patients in $T_3M_0M_0$ phase. But the negativity of the CRM was encountered in 84.3 % and 85.8 % cases in the patients not mentioned to have intact lymph nodes over both groups correspondingly (42.9 % comparing to N+). Thus, statistical exact differences appeared in the CRM status depending on whether metastatic lymph nodes existed or not within the group.

The phase of the carcinoma disease affects the CRM status as it affects the tactics of treatment. Our observations show that the positivity of the CRM practically equals to zero in I phase. The CRM became positive in only 1 patient of LTME group in I phase (14.2 %). But the CRM always became negative in the OTME group. The CRM became positive in 25 % cases and negative in 75 % cases in the LTME and OTME groups in II phase. But the CRM became positive in 42.8 % and 45.7 % cases and negative in 57.2 % and 54.3 % cases in the LTME and OTME groups in III phase. There was not statistical exact difference with regard to the CRM status depending on the phase among the groups. Statistical exact differences were noted in the CRM status depending on the phase within the group. The probability of the CRM to be positive increases as the phase of the disease increases.

We investigated the effect of the location of the mass on the CRM in our research work by considering the effects of the TME quality in the localization of the tumor. In case the mass is located in the distance of 0-6 cm, the CRM became 61.5 % in the LTME group, 62.5 % in the OTME group, 38.5 % in the positive LTME group but 37.5 % negative in the OTME group. The CRM became positive by 55.5 % in the LTME group and 54.5 % in the OTME group in the masses locating in the middle region of the rectum. But the CRM became negative in 44.5 % and 45.5 % cases. But the CRM became totally 31.2 % positive in the LTME group and negative in 68.8 % cases (22.2 % positive in the OTME group) when the rectal carcinoma is located in the distance of >12 cm. The same index became by 77.8 % in the OTME group. It is seen that the lower the mass, the higher the probability of positivity of the CRM. If it is connected with the anatomic properties of the same zone on one hand, it is connected with the restriction of the opportunities of the laparoscopic technology in the masses located below on the other hand. Our observations show that serious difference exists among the OTME and LTME groups of the middle and superior rectal masses with regard to the CRM status. Though difference is found between the LTME and OTME groups of the inferior rectal masses, the same difference is not statistically exact. And there were disclosed differences assuming statistical importance in both the OTME group and LTME group within the group. The probability of positivity of the CRM was high in the inferior rectal masses. The high level of the CRM positivity in the inferior rectal masses in the LTME group includes the use of this technology in the groups of patients with high practice and selection but not application of laparoscopic technology in this group of patients as counteraction. The effect of the size of tumor on the CRM was also proved in our investigations. As the physical sizes of the tumor increases, the

probability of positivity of the CRM also increases. The tumor size changed from 10 mm to 100 mm. We divided the masses into 3 groups according to their sizes: 1–3 cm masses in small size, 4–6 cm in middle size and 7–10 cm in large size. As the tumor size increases, the probability of positivity of the CRM also increases. The CRM is quite negative in small-sized masses in some cases. The distribution of the patients in the LTME and OTME groups according to the largest diametric size of tumor and the effect of the size of tumor on the CRM status are following.

3 out of 12 patients (small-sized) including in the LTME group were in T_1 phase, 9 in T_2 phase, 2 out of 23 (middle-sized) patients in T_2 phase and 21 in T_3 phase, 4 out of 12 (large-sized) patients in T_4 phase and 8 in T_3 phase. As it is seen, correlation has never existed between the size of tumor and its phase. The sizes of tumor were larger in the patients included in the OTME group than those in the LTME group. It did not affect the positivity of the CRM in the same group of patients so much. The main reason for it, is connected with being easier of removing of large-sized masses in an open way. The probability of positivity of the CRM in the cases of being smaller of the tumor size is 8.3 % and 10 % in the LTME and OTME groups but the probability of negativity of the CRM is 91.6 % and 90 % respectively. The probability of positivity of the CRM in the medium-sized masses over both groups is 58.3 % and 53.5 % but the probability of negativity is 41.7 % and 46.5 % respectively. The CRM became positive in the large-sized masses in 90.9 % case in the LTME group but 94.4 % in the OTME group; but negative in 9.1 % and 5.6 % cases. Though differences are observed between the groups, statistic dynamism was not followed between these differences. But differences of statistical importance were noted within the group.

The CRM became positive in 25.0 % and negative in 16.1 % cases while performing the low quality TME in the LTME group. The appropriate indexes were 24.2 % and 17.4 % in the Grade 1 in the OTME group. Though differences are observed among the groups with regard to the positivity and negativity of the CRM, they are not statistically correct. The CRM became positive in 25.6 % in the Grade 2 in the LTME group. This case was connected with both the technical errors observed during the surgical intervention and being of the surgical clearance of the tumor process >1 mm in connection with it. The appropriate index became 27.3 % and 43.5 % in the OTME group. Though differences are disclosed among the groups, they were not statistically correct. The CRM positive cases were noted in the Grade 3. Noting of such a case was directly connected with the disease itself. The CRM became positive in 50 % cases and negative in 51.6 % in the LTME group; but the appropriate index became 48.5 % and 39.1 % in the OTME group.

Thus, despite of the lack of serious differences between the groups, differences happened in the CRM status irrespective of the TME quality within this group. The probability of positivity of the CRM was disclosed in the condition of existing of the metastatic lymph nodes where the depth of the invasion increased during the test of the factors affecting the CRM status together. We have already mentioned some aspects of these relationships in our previous studies [7].

If low quality TME was conducted during the operation, the probability of radicalism of the surgical intervention became lower than the Grade 3. It shows the fact that the quality of the TME is more important than the other factors in respect of the CRM status. Thus, the errors made in the surgical technique are the most important factor increasing the probability of local recurrence. In contrast to that the technique of a surgical operation (laparoscopic, open) does not affect the CRM status as the factors creating statistical exact difference with the factors like the distance from the tumor to the anus. Our results are consistent with the data of Cernikovskij IL, who also found no statistically significant difference in surgical technique in influencing treatment outcomes [2].

However, there are opposing views in the available literature. So, randomized prospective trials of laparoscopic rectus resections intestines (CLASICC, COLOR II, COREAN) showed significantly less blood loss, earlier recovery of bowel function and a shorter inpatient stay compared to open interventions. But the quality of TME has not any differences between open and laparoscopic way, as in our study [8, 9, 12].

Dauletbayev DA et al. also came to the conclusion that laparoscopic surgery for colorectal cancer has a number of advantages compared to the traditional one, The authors are convinced that in the near future minimally invasive radical operations in oncological practice will occupy an increasingly high position in the structure of surgical interventions in patients with colorectal cancer [1]. But we agree with authors that laparoscopic surgery requires additional detailed development of the intervention technique.

It is assumed a special interest to study the relationship between the parameters mentioned by considering the relationship between the radicalism of the surgical intervention and quality of the TME. Such as, the errors made in the TME technique have a direct effect on the CRM status. But the low quality of the TME does not mean the positivity of the CRM in full. The low quality TMEs in the masses of T_1 and T_2 phase is not always resulted in producing of local recurrence of the tumor. On the contrary, the CRM may seriously be positive in T_3, especially T_4 masses despite of performing of the TME in high

quality. Therefore, it should not be forgotten that there may sometimes be right and sometimes wrong correlation between the TME quality and the CRM status and this shade should be considered while selecting the tactics of treatment.

Conclusion

1. The depth of invasion to the quality of the preparation made, is affected by the distance of the tumor from the anus. These differences are statistically correct. But the differences happened in the surgical technique are not statistically correct.

2. The status of the regional lymph nodes, the phase of carcinoma and the technique of surgical operation do not affect the TME quality in a statistic right way.

3. The factors like the size of tumor, depth of invasion, metastatic damage of mesorectal lymph nodes, distance from anus, phase of tumor process and TME quality do not have statistical right effect on the CRM status during the pathohistological examination of the preparation made.

4. The CRM is affected by the factors like a) development of the tumor out of the intestinal wall, b) metastatic damage of lymph nodes, c) existence of tumor embolus and deposits, d) TME quality as a result of testing of the affecting factors together.

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