South Russian Journal of Cancer 2020, v.1, №2, p. 22-27
https://doi.org/10.37748/2687-0533-2020-1-2-3

ORIGINAL ARTICLE

MINIMALLY INVASIVE SURGERY IN TREATMENT OF PATIENTS WITH METASTATIC COLORECTAL CANCER

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ABSTRACT

Purpose of the study. Was to improve the results of treatment for metastatic colorectal cancer using laparoscopic surgical technologies.

Patients and methods. We analyzed the data on 311 patients aged 44–78 years with colorectal cancer and liver metastases; in 2005–2015, all patients received treatment at National Medical Research Centre for Oncology of the Ministry of Health of Russia. The main group included 161 patients with metastatic colon cancer and resectable liver metastases receiving laparoscopic surgery; 150 patients with the same disease receiving open surgery were controls.

Results. The study demonstrated that laparoscopy with a combination of developed surgical techniques significantly (p<0.05) reduced the number of surgical complications in the main group (1.8%) compared to controls (12.8%). Patients with metastatic colorectal cancer receiving laparoscopy demonstrated higher, compared to patients with standard open surgery, relative risks of cardiovascular and respiratory complications (HR=4.7, p=0.001), thrombohemorrhagic complications (HR=2.8, p=0.05) and arrhythmia (HR=3.73, p=0.07), but lower risks of surgical complications (HR=0.13, p=0.001). Survival of patients with metastatic colorectal patients was statistically significantly higher in the main group compared to controls: log-rank test = 2.11 at p=0.035.

Conclusions. Laparoscopy reduced the number of surgical complications, compared to open surgery. However, patients with comorbid pathologies showed higher relative risks of other complications.

Keywords:
colorectal cancer, surgical treatment, laparoscopic surgery, liver metastasis, comorbid disease, surgical complications

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Information about funding: no funding of this work has been held.
Conflict of interest: authors report no conflict of interest.

For citation:
Gevorkyan Yu.A., Kolesnikov V.E., Soldatkina N.V., Kharagezov D.A., Dashkov A.V., Kaymakchi D.O., Mirzoyan E.A., Poluektov S.I., Tolmakh R.E., Stateshny O.N., Doncov V.A. Minimally invasive surgery in treatment of patients with metastatic colorectal cancer. South Russian Journal of Cancer. 2020; 1(2): 22-27. https://doi.org/10.37748/2687-0533-2020-1-2-3

Received 28.12.2019, Review (1) 14.02.2020, Review (2) 11.03.2020, Accepted 01.06.2020

Южно-российский онкологический журнал 2020, т.1, №2, с. 22-27
https://doi.org/10.37748/2687-0533-2020-1-2-3
ОРИГИНАЛЬНАЯ СТАТЬЯ

МАЛОИНВАЗИВНЫЕ ХИРУРГИЧЕСКИЕ ВМЕШАТЕЛЬСТВА В ЛЕЧЕНИИ БОЛЬНЫХ МЕТАСТАТИЧЕСКИМ КОЛОРЕКТАЛЬНЫМ РАКОМ

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РЕЗЮМЕ

Цель исследования. Улучшение результатов лечения метастатического колоректального рака с использованием лапароскопического метода.

Пациенты и методы. Проводился анализ историй 311 пациентов с раком ободочной и прямой кишки, имеющих метастатические очаги в печени, которые проходили лечение в ФГБУ «НМИЦ онкологии» Минздрава России в период с 2005 по 2015 гг. Возраст больных от 44 до 78 лет. В основную группу вошел 161 пациент с резектабельными очагами в печени, которым были выполнены лапароскопические оперативные вмешательства. Контрольную группу составили 150 человек, перенесших открытые операции.

Результаты. Было доказано, что лапароскопический доступ с применением разработанных хирургических методик позволил достоверно снизить частоту послеоперационных хирургических осложнений у пациентов в основной группе (1,8%) по сравнению с контрольной (12,8%; $p<0,05$).

Использование лапароскопического доступа по сравнению с открытым позволило снизить риск хирургических осложнений (ОР=0,13; $p=0,001$), однако привело к увеличению развития осложнений со стороны сердечно-сосудистой и дыхательных систем (ОР=4,7; $p=0,001$), аритмий (ОР=3,73; $p=0,07$), тромбогеморрагических осложнений (ОР=2,8; $p=0,05$). Выживаемость в основной группе была статистически значимо выше, логарифмический ранговый критерий составил 2,11 при $p=0,035$.

Заключение. Лапароскопический доступ позволил сократить число хирургических осложнений по сравнению с открытыми операциями. Однако у больных, имеющих коморбидную патологию, выше относительный риск развития осложнений со стороны других органов и систем.

Ключевые слова:
колоректальный рак, хирургическое лечение, лапароскопическая хирургия, метастатическое поражение печени, коморбидная патология, хирургические осложнения.

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Информация о финансировании: финансирование данной работы не проводилось.
Конфликт интересов: авторы заявляют об отсутствии конфликта интересов.

Для цитирования:
Геворкян Ю.А., Колесников В.Е., Солдаткина Н.В., Харагезов Д.А., Дашков А.В., Каймакчи Д.О., Мирзоян Э.А., Полуэктов С.И., Толмах Р.Е., Статешный О.Н., Донцов В.А. Малоинвазивные хирургические вмешательства в лечении больных метастатическим колоректальным раком. Южно-российский онкологический журнал. 2020; 1(2): 22-27. https://doi.org/10.37748/2687-0533-2020-1-2-3

Получено 28.12.2019, Рецензия (1) 14.02.2020, Рецензия (2) 11.03.2020, Принята к печати 01.06.2020

Colorectal cancer ranks third in the structure of overall cancer incidence [1]. However, despite the entire Arsenal of modern diagnostic methods, 25% of the initial examination have stage IV of the process, with the presence of metastatic foci in the liver [2]. The standard therapy for such patients is combined and complex treatment using both surgical and medicinal methods [3]. The use of drug therapy contributes to the transition of unresectable tumors to resectable ones [4,5,6].

The best way to obtain satisfactory treatment results for such patients is to resect liver tumors [7,8,9]. Recently, laparoscopic access has become the main method of surgery for metastatic colorectal cancer [10,11]. In the literature, there is more information about synchronous resections of the primary focus and liver metastases [12,13]. The advantages of this method are confirmed by randomized studies [14,15,16]. Low trauma is the main advantage in laparoscopy, but despite this, this access for individual patients remains an alternative to open interventions.

Objective: to improve the results of treatment of metastatic colorectal cancer by using laparoscopic techniques.

PATIENTS AND METHODS

We studied data on 311 patients with colon and rectal cancer who have metastatic foci in the liver. The age of patients was 44–78 years. The main group included 161 patients who underwent laparoscopic access, and the control group included 150 patients who underwent open operations. All patients received the treatment at National Medical Research Centre for Oncology of the Ministry of Health of Russia the period from 2005 to 2015. Inclusion criteria: the patient's consent to participate in this study, the absence of concomitant pathology in the stage of exacerbation or decompensation, the presence of verification of processes, resectability of metastases. In the main group of patients with sigmoid colon cancer and liver metastases, a retractor was used to mobilize the sigmoid colon (RF patent for utility model no. 2489150 of 10.08.2013, bul. no. 22: "Retractor for sigmoid colon mobilization"). In all groups, when selecting a linear cross-linking device, the method of measuring the wall thickness of the organs being stitched using a special reusable meter was used (received a patent for a utility model No. 186083 from 28.12.2018 "Device for measuring during minimally invasive endoscopic interventions").

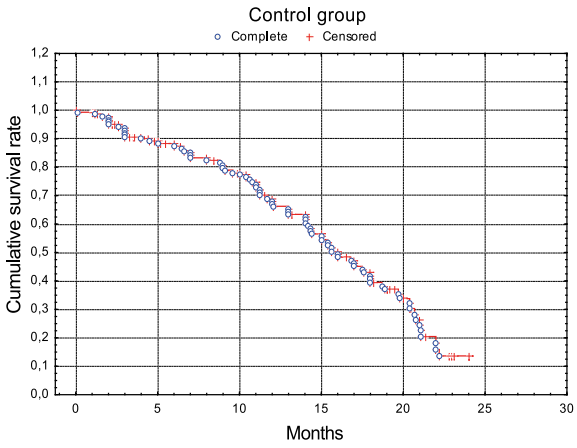

Fig. 1. Overall survival of patients in the control group for two years after the operation. Complete – fatal outcome, Censored – pending case

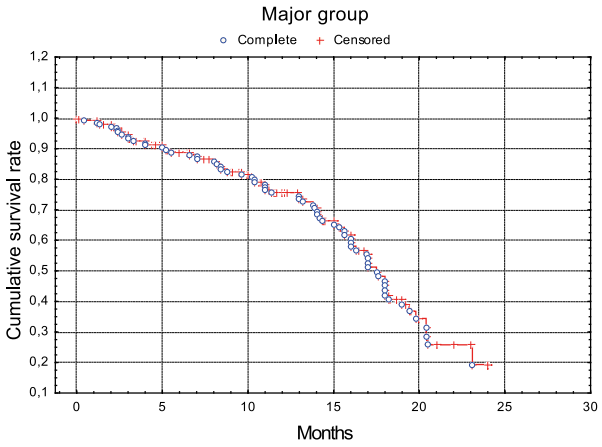

Fig. 2. Overall survival of patients in the main group for two years after the operation. Complete – fatal outcome, Censored – pending case

In the main and control groups of the study, women (52.7 and 54.3%, respectively) were more numerous than men (47.3% and 45.7).

Both in the main and control groups, patients with rectal pathology were more common (35.3% and 32.7%, respectively). All patients had adenocarcinoma, but the majority were patients with low-grade adenocarcinoma (65.3% in the main group and 71.8% in the control group). All patients in the groups had stage IV disease (T2–4N1M1). Often performed surgical intervention, both in the main and control groups were: sigmoid colon resection (31.1 and 33.3%), anterior rectal resection (23.4% and 22.5%, respectively). Anatomic liver resections were performed more often in the main group, and atypical liver resections were performed in the control group. Statistical data processing was performed using the software Statsoft Statistica 10.0. The Shapiro-Wilk W-test is used to estimate the normality of the distribution.

THE RESULTS OF THE STUDY AND DISCUSSION

The number of postoperative complications in the control group was 34 (21.1%), and in the main group — 22 (14.7%). The use of laparoscopic access compared to open access reduced the risk of surgical complications (HR=0.13, *p*=0.001) on the one hand, but on the other led to an increase in the development of complications from the cardiovascular and respiratory systems (HR=4.7, *p*=0.001), arrhythmias (HR=3.73, *p*=0.07), thrombohemorrhagic complications (HR=2.8, *p*=0.05)

The total number of complications in the main groups was 42% (68 patients), in the control group — 29% (44 patients). Hospital complications in the main group developed in 34 (21.1%) patients, in the control group — in 22 (14.7%) patients. Complications related to the cardiovascular and respiratory systems in the main group were observed in 20 (12.4%), and in the control group in 4 (2.7%; *p*=0.001). In the main group, 12 (7.5%) had thrombohemorrhagic complications, and 4 (2.7%) in the control group. Complications associated with drug removal in the control group were observed in 2 (1.2%), and in the control group — in 14 (9.3%; *p*=0.001). Thus, an increase in the number of postoperative complications in the main group of patients was observed due to an increase in the number of complications associated with the cardiovascular and respiratory systems. This is probably due to the need to apply carboxyperitoneum in patients with premorbid pathology of the cardiovascular and respiratory systems when performing laparoscopic surgery.

In the structure of postoperative complications, pneumonia was found in 7 patients in the main group (4.3%), and in the control group in 1 patient (0.7%; *p*=0.04). Acute myocardial infarction occurred in 2 patients (1.2%) in the main group — in 1 (0.7%; *p*=0.60).

PE was observed only in the main group in 3 (1.9%), (*p*=0.09), and mesenteric thrombosis in 1 (0.7%) patient from the control group (*p*=0.29). Deep vein thrombosis in the main group was in 9 patients (5.6%), and in the control group in 3 (2.0%; *p*=0.10). Acute cerebrovascular accident was observed in 1 person (0.6%) from the main group (*p*=0.33), and hypertensive crisis in 4 patients from the main group (2.5%; *p*=0.05). Arrhythmias were more common in the main group in 8 patients (5.0%; *p*=0.08), and infectious wound complications at the site of intervention in the control group — in 7 (4.7%; *p*=0.007). Intra-abdominal bleeding was observed in the control group in 2 (1.3%), and in the main group in 1 (0.6% (*p*=0.52). Peritonitis associated with anastomosis failure in the control group was 4 (2.7%), and in the main group 1 (0.6%; *p*=0.16). Relaparotomy was performed only in the control group-in 7 patients- (4.7%; *p*=0.007). Repeated laparoscopy was performed in 3 patients (1.9%) from the main group (*p*=0.09). Bile congestion was in 1 patient (0.6%) from the main group (*p*=0.29), and eventeration in 5 (3.3%) from the control group (*p*=0.7). Hospital mortality in the main and control groups was the same (5 and 6%, respectively).

Overall survival of patients in all groups was monitored for 24 months after surgery. Figure 1 shows the 2-year overall survival of patients in the control group.

In the main group, a decrease in the survival rate from 1.0 to 0.23 was observed for 2 years

after laparoscopic operations. In the group of patients using laparoscopic access, there is an increase in overall survival, compared to the group of patients using open traditional access.

CONCLUSIONS

1.Laparoscopic access in combination with the developed surgical techniques allowed to significantly reduce the frequency of infectious and inflammatory postoperative complications in the main group (p<0.05).

2. the use of laparoscopic access compared to open access reduced the risk of surgical complications (HR=0.13, p=0.001), but led to an increase in the development of complications from the cardiovascular and respiratory systems (HR=4.7, p=0.001), arrhythmias (HR=3.73, p=0.07), thrombohemorrhagic complications (HR=2.8, p=0.05).

3. in patients in the main group, compared with the control group, there is an increase in overall survival (the logarithmic rank criterion was 2.11 at p=0.035)

SUMMARY

Colorectal cancer ranks fourth in the structure of total cancer mortality. In 25% of patients have stage IV at the first treatment, with primary liver damage. The standard of treatment for such patients is combined and complex treatment.

In recent years, laparoscopic surgery for metastatic colorectal cancer has become a priority. In our study, it was proved that the use of laparoscopic access reduced the number of surgical complications compared to open operations. However, despite this, patients with comorbid pathology have a higher relative risk of developing complications from other organs and systems.

Authors contribution:

Gevorkyan Yu.A. – editing of the work.

Kolesnikov E.V., Kharagezov D.A., Dashkov V.A. – the literature review.

Soldatkina N.V. – literature review, responsible for the scientific and technical level of work.

Kaymakchi D.O., Mirzoyan A.E., Poluektov S.I., Tolmakh R.E., Stateshny O.N., Doncov V.A. – conducted analysis of data on patients treated in the National Medical Research Centre for Oncology of the Ministry of Health of Russia.

References

1. Adam R, de Gramont A, Figueras J, Kokudo N, Kunstlinger F, Loyer E, et al. Managing synchronous liver metastases from colorectal cancer: a multidisciplinary international consensus. Cancer Treat Rev. 2015 Nov; 41(9): 729–741. https://doi.org/10.1016/j.ctrv.2015.06.006

2. Cheung TT, Poon RTP. Synchronous resections of primary colorectal tumor and liver metastasis by laparoscopic approach. World Journal of Hepatology. 2013 Jun 27; 5(6): 298–301. https://doi.org/10.4254/wjh.v5.i6.298

3. Eadens MJ, Grothey A. Curable metastatic colorectal cancer. Curr Oncol Rep. 2011 Jun; 13(3): 168–176. https://doi.org/10.1007/s11912–011–0157–0

4. Kit OI, Gevorkyan YuA, Soldatkina NV, Kolesnikov VE, Kharagezov DA, Dashkov AV, et al. Minimally invasive technologies in the complex treatment of colorectal cancer with liver metastases. Coloproctology. 2014; S3(49): 65–66. (In Russian).

5. Papa A, Rossi L, Lo Russo G, Giordani E, Spinelli GP, Zullo A, et al. Emerging role of cetuximab in the treatment of colorectal cancer. Recent Pat Anticancer Drug Discov. 2012 May 1; 7(2): 233–247. https://doi.org/10.2174/157489212799972882

6. Tsujii M. Search for novel target molecules for the effective treatment or prevention of colorectal cancer. Digestion. 2012; 85(2): 99–102. https://doi.org/10.1159/000334678

7. Alekhnovich VYu, Prokhorov AV. Comparative analysis of comprehensive treatment of metastatic colorectal cancer. Medical Journal. 2018; 2 (64): 21–26. (In Russian).

8. Kit OI, Gevorkyan YuA, Kolesnikov VE, Soldatkina NV, Kharagezov DA, Kaimakchi OYu. Laparoscopic combined resection of sigmoid colon, panhysterectomy with removal through vagina stump. Pirogov Russian Journal of Surgery Surgery. Journal named after N. I. Pirogova. 2014;(11): 63–65. (In Russian).

9. Kit OI, Gevorkyan YuA, Soldatkina NV, Kharagezov DA, Kolesnikov VE, Milakin AG. Multiple primary colorectal cancer: the

possibilities of minimally invasive surgical interventions. Coloproctology. 2017; 1(59): 38–42. (In Russian).

10. Efanov MG, Alikhanov RB, Tsvirkun VV, Kazakov IV, Kim PP, Van'kovich AN, et al. Early and Long-term Outcomes of Laparoscopic and Robot-assisted Liver Resections. Specialized Center's Experience. Annals of HPB Surgery. 2018; 23(1): 38–46. (In Russian). https://doi.org/10.16931/1995–5464.2018138–46

11. Kit OI, Gevorkyan YuA, Soldatkina NV, Kolesnikov EN, Kolesnikov VE, Kozhushko MA, et al. Combined surgery for locally advanced colorectal cancer. Pirogov Russian Journal of Surgery Khirurgiya. Zhurnal imeni N. I. Pirogova. 2016;(11): 42–47. (In Russian). https://doi.org/10.17116/hirurgia20161142–47

12. Hoekstra LT, Busch ORC, Bemelman WA, van Gulik TM, Tanis PJ. Initial experiences of simultaneous laparoscopic resection of colorectal cancer and liver metastases. HPB Surg. 2012; 2012: 893956. https://doi.org/10.1155/2012/893956

13. Hatwell C, Bretagnol F, Farges O, Belghiti J, Panis Y. Laparoscopic resection of colorectal cancer facilitates simultaneous surgery of synchronous liver metastases. Colorectal Dis. 2013 Jan; 15(1): e21–28. https://doi.org/10.1111/codi.12068

14. Gunka I, Dostalik J, Martinek L, Gunkova P, Mazur M, Vavra P. Long-term results of laparoscopic versus open surgery for nonmetastatic colorectal cancer. Acta Chir Belg. 2012 Apr; 112(2): 139–147. https://doi.org/10.1080/00015458.2012.11680812

15. van der Pas MH, Haglind E, Cuesta MA, Fürst A, Lacy AM, Hop WC, et al. Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. Lancet Oncol. 2013 Mar; 14(3): 210–218. https://doi.org/10.1016/S1470–2045(13)70016–0

16. Slesser AAP, Simillis C, Goldin R, Brown G, Mudan S, Tekkis PP. A meta-analysis comparing simultaneous versus delayed resections in patients with synchronous colorectal liver metastases. Surg Oncol. 2013 Mar; 22(1): 36–47. https://doi.org/10.1016/j.suronc.2012.11.002

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