

INTRAOPERATIVE PHOTODYNAMIC THERAPY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY IN CYTOREDUCTIVE TREATMENT OF PATIENTS WITH DISSEMINATED MUCINOUS CARCINOMA OF APPENDIX

Sidorov D.V., Grishin N.A., Lozhkin M.V., Troitsky A.A., Moshurov R.I., Bykasov S.A., Urlova A.N., Filonenko E.V.

P.A. Herzen Moscow Oncology Research Center – branch of FSBI NMRRС of the Ministry of Health of the Russian Federation, Moscow, Russia

Abstract

The article presents the experience of surgical treatment of 57 patients with peritoneal pseudomyxoma of appendicular genesis. In 32 (56.1%) patients, the operation was supplemented with intraoperative photodynamic therapy (IOPDT). In the other 25 (43.9%) patients, hyperthermic intraperitoneal chemotherapy (HIPEC) was performed. The analysis according to the value of the peritoneal carcinomatosis index, completeness of cytoreduction, the volume of operations performed, postoperative complications and hospital mortality, as well as long-term treatment results in two groups is presented. It was shown that with significantly worse results in terms of cytoreduction completeness obtained in the IOPDT group compared to the HIPEC group, the 5-year survival rate in the HIPEC group was 86.6%, with IOPDT - 65.2%. At the same time, in the IOPDT group, the rate of postoperative complications was significantly lower (11.1%), and there was no mortality; in the HIPEC group, these indicators were 23.8% and 12.0%, respectively. The results obtained indicate that the IOPDT method is an effective and promising direction in the surgical treatment of peritoneal pseudomyxoma.

Keywords: peritoneal pseudomyxoma, photodynamic therapy, hyperthermic chemotherapy, peritoneal carcinomatosis index, cytoreductive surgery.

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Contacts: Grishin N.A., grishinlap@mail.ru

ИНТРАОПЕРАЦИОННАЯ ФОТОДИНАМИЧЕСКАЯ ТЕРАПИЯ И ГИПЕРТЕРМИЧЕСКАЯ ВНУТРИБРЮШНАЯ ХИМИОТЕРАПИЯ ПРИ ЦИТОРЕДУКТИВНОМ ХИРУРГИЧЕСКОМ ЛЕЧЕНИИ БОЛЬНЫХ ДИССЕМНИРОВАННОЙ МУЦИНОЗНОЙ КАРЦИНОМОЙ АППЕНДИКСА

Д.В. Сидоров, Н.А. Гришин, М.В. Ложкин, А.А. Троицкий, Р.И. Мошуров, С.А. Быкасов, А.Н. Урлова, Е.В. Филоненко

МНИОИ им. П.А. Герцена – филиал ФГБУ «НМИЦ радиологии» Минздрава России, Москва, Россия

Резюме

В статье представлен опыт хирургического лечения 57 больных псевдомиксомой брюшины аппендикулярного генеза. У 32 (56,1%) пациентов операция дополнена интраоперационной фотодинамической терапией (ИОФДТ), у других 25 (43,9%) больных проведена

гипертермическая внутрибрюшная химиотерапия (ГИВХ). Представлен анализ по величине индекса перитонеального канцероматоза, полноте циторедукции, объему выполненных операций, послеоперационным осложнениям и госпитальной летальности, отдаленным результатам лечения в двух группах. Показано, что при достоверно худших результатах по показателям полноты циторедукции, полученных в группе ИОФДТ по сравнению с группой ГИВХ, 5-летняя выживаемость в группе с ГИВХ составила 86,6%, с ИОФДТ – 65,2%. При этом в группе ИОФДТ был достоверно ниже показатель послеоперационных осложнений (11,1%) и отсутствовала летальность, в группе ГИВХ эти показатели составили 23,8% и 12,0%, соответственно. Полученные результаты свидетельствуют о том, что метод ИОФДТ является эффективным и перспективным для использования при хирургическом лечении псевдомиксомы брюшины.

Ключевые слова: псевдомиксома брюшины, фотодинамическая терапия, гипертермическая химиотерапия, индекс перитонеального канцероматоза, циторедуктивная операция.

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Контакты: Гришин Н.А., grishinlap@mail.ru

Introduction

Tumors of the vermex account for less than 1% of all malignant neoplasms. The most common morphological forms of tumors of this localization are mucinous carcinomas (about 50%), intestinal adenocarcinomas (10%), signet ring cell carcinoma and neuroendocrine tumors [1]. The progression of low-grade mucinous neoplasia leads to the development of peritoneal pseudomyxoma, which is currently considered a clinical syndrome, rather than a pathomorphological definition. In pseudomyxoma, mucinous masses of different densities (soft, semi-hard, hard) accumulate in the abdominal cavity with a different ratio of tumor cells and different degree of invasion into the parietal and visceral sheets of the peritoneum [2]. In the 8th edition of the TNM Classification of Malignant Tumors, in the determination of the stage of mucinous tumors of the appendix, the primary tumor is assessed from T4a to T4b; distant metastases: M1a: peritoneal, mucin only, without tumor cells, and M1b: peritoneal mucinous carcinomatosis [3]. Regional lymph nodes involvement is hardly ever observed in this disease. Cytoreductive surgery in patients with low-grade mucinous tumors allows achieving 5-year survival rates of 50-85%, depending on the TNM level of the process. In cases of non-mucinous adenocarcinomas of the appendix, the indicator does not exceed 10% [4]. In recent years, a number of authors suggest using photodynamic therapy, which produces a multivariate antitumor response, to increase the effectiveness of cytoreductive surgery [5–8].

We present our experience of surgical treatment of peritoneum pseudomyxoma with the use of intraoperative photodynamic therapy (IOFDT) and hyperthermic intraperitoneal chemotherapy (HIPEC).

Materials and methods

Surgical treatment was performed in 57 patients with peritoneum pseudomyxoma of appendiceal origin. The criteria for inclusion in the study were verified mucinous neoplasia of the appendix after appendectomy or the morphological pattern of pseudomyxoma obtained by biopsy, as well as the absence of other types of abdominal and pelvic tumor pathology. The majority of patients were female (40 people). The age of patients ranged from 25 to 79 years, the average age being 52.5 ± 11.7 years, the majority of patients belonged to the capable to work and socially active population. In 32 (56.1%) patients, cytoreductive surgery was supplemented with IOFDT, in 25 (43.9%), with HIPEC. There were no significant differences between the study groups in terms of gender and age. Almost a third (29.2%) of patients had previously undergone abdominal surgery, including for pseudomyxoma. The prevalence of the process was estimated by the value of the peritoneal carcinomatosis index (PCI). We used the methods developed at P. A. Hertsen Moscow Oncology Research Center for determining CT PCI and ultrasound PCI, on the basis of which the involvement of each of the 13 sectors of the abdominal cavity was evaluated, as well as the PCI score, the maximum value of which was 39. At low $PCI \leq 5$, diagnostic fluorescence laparoscopy was performed. The diagnostic task was not only to determine the PCI value, but also to plan the surgery taking into account the degree of damage to the visceral peritoneal layer, the involvement of elements of the hepatoduodenal ligament and lesser peritoneal sac, as well as the expected scope of cytoreduction.

The specifics of the surgical stage

Surgical intervention began with dissection of the skin, subcutaneous tissue and the aponeurosis along

the white line, without opening the abdominal cavity, if possible. With an electric knife, the peritoneum was separated from the transverse fascia and the posterior layer of the aponeurosis of the rectus muscles as laterally and dorsally as possible, up to the lumbar muscles. Defects of the peritoneal lamina were sutured to avoid the leakage of fluid or mucinous masses. If the changes in the parietal peritoneum were not pronounced, it was mobilized together with the connective tissue structures of the anterior abdominal wall, leaving aponeurotic tape about 1 cm wide at the edges of the incision for subsequent suturing. The upper limit of the mobilization of the parietal peritoneum was the diaphragm, the lower being the bladder and the Douglas pouch. After that, laparotomy was performed. After removal of mucin of various fractions and aspiration of ascitic fluid, the abnormal large omentum underwent subtotal resection or extirpation. Then the colon and the rectosigmoid colon were mobilized in the same way as in subtotal colectomy. In pseudomyxoma, either right-sided hemicolectomy or appendectomy was performed, depending on the degree of changes in the appendix and the dome of the cecum, as well as the scope of involvement. The parietal peritoneum was removed acutely in three parts: the peritoneum of the right lateral canal and the right half of the diaphragm, the left lateral canal with the remaining part of the peritoneum of the diaphragm, and the pelvic part with the visceral layer, starting from the mesenteric root. All tumor implants were removed from the peritoneal omental sac, the Douglas pouch, and the liver capsule, and, when necessary, the abdominal and pelvic organs were resected or removed.

The basis of cytoreductive surgery for carcinoma-tosis is the maximum possible removal of the parietal layer of the peritoneum, i. e., subtotal parietal peritonectomy, the lesion of the visceral layer being the main obstacle to optimal cytoreduction. The organs that are most frequently extirpated include the uterus with appendages, the spleen, the right half of the colon, and the appendix. Given the specifics of the tumor cells spread, resection of the right dome of the diaphragm and the bladder was necessary in more than half of the cases. The key question in the case of a preserved appendix is the choice of the scope of intervention for its tumor, i. e., right-sided hemicolectomy or appendectomy. It is necessary to take into account the PCI value and the tumor involvement of the caecum.

The intraoperative photodynamic therapy method

IOFDT was performed according to the method developed at the P. Herzen MORC. Two drugs were used as photosensitizers: photohem and photosense. The first was administered intravenously 48 hours before

surgery at a dose of 2.5 mg per kg of body weight, the second was 2-8 hours before the start of the radiation session at a dose of 0.2 mg per kg of body weight. A strict light regime was observed by the patients for 4 or 8 weeks, for photohem and photosens, respectively. During the IOFDT session, the abdominal cavity walls, the areas of the parietal peritoneum remaining after surgery, and the organs that were affected but not resected (the stomach, the bladder, the spleen), as well as the edges of the laparotomic wound, were exposed to radiation. To perform the manipulation, a laser installation LFT-630/675-01-Biospec (OOO "Biospec", Russia) was used, with a wavelength of 630 nm (for photohem) and 672 nm (for photosense), a special transducer with an outer diameter of 10 mm, through which a cylindrical diffuser with a diameter of 1.5 mm was passed. At a distance of 2.5 cm from the distal end of the transducer, a special opening is cut on $\frac{1}{2}$ of the circumference. The use of this design made it possible to provide the desired direction of the light flow. The colon and the loops of the small intestine were protected by a special light-tight cloth. Sequentially, with the overlap of the light fields, all accessible abdominal areas were treated, on average, about 20 positions with 2.5 minutes exposure for each. The power density of the light energy ranged from 6 to 10 J/cm². The "blind" part of the transducer was constantly turned to the loops of the small intestine in order to avoid their specific damage. However, taking into account the time of the resection stage, the visceral peritoneum also received a therapeutic dose of laser radiation.

Hyperthermic intraoperative intraperitoneal chemotherapy method

HIPEC was performed after the completion of the surgical stage, with the use of Coliseum (open) technique. The edges of the wound were attached with ligatures on a circular wound dilator, and more recently on a multi-functional THOMPSON wound retractor. We used the SunCHIP device (GamidaTech, France). As a cytostatic agent, cisplatin was used at a dose of 100 mg/m² per 400 ml of saline solution. The operating temperature at the inlet was 43-44°C, at the outlet, 42-43°C. The procedure with the use of the chemical product lasted 60 minutes. During the treatment, the temperature regime in various parts of the abdominal cavity and the patency of the drainage tubes were carefully monitored. Given the cytoreductive nature of the surgery, a large number of small fragments of adipose tissue remain in the abdominal cavity, despite its preliminary sanitation, which disrupts the drainage function of the system and thereby causes local hyperthermia in certain areas of the abdominal cavity. Body temperature was monitored with esophageal and skin sensors, preventing it from rising above 39.5°C.

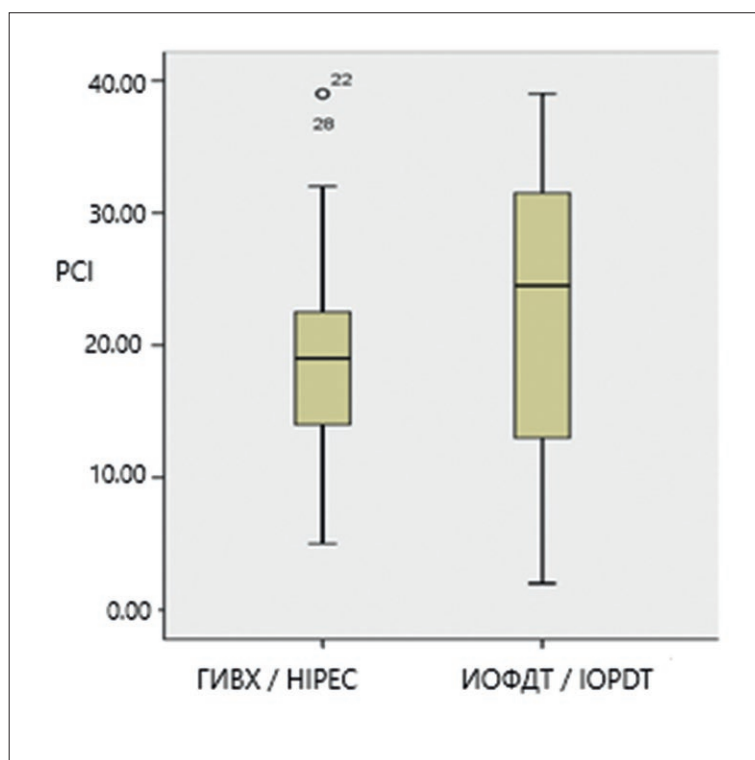


Рис. 1. Распределение больных по PCI
Fig. 1. Distribution of patients by peritoneal carcinomatosis index

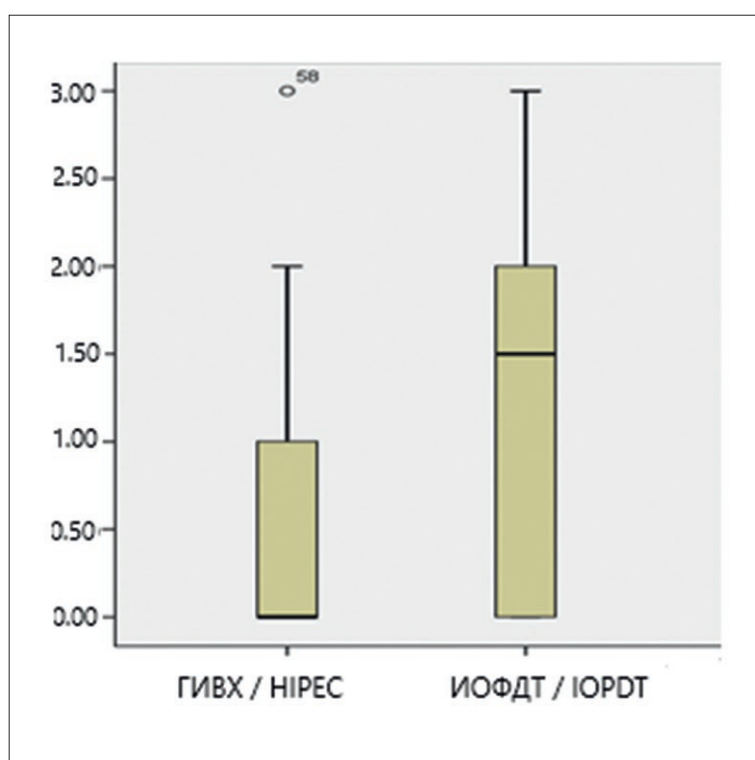


Рис. 2. Распределение больных по полноте выполненных циторедуктивных операций
Fig. 2. Distribution of patients according to the completeness of performed cytoreductive operations

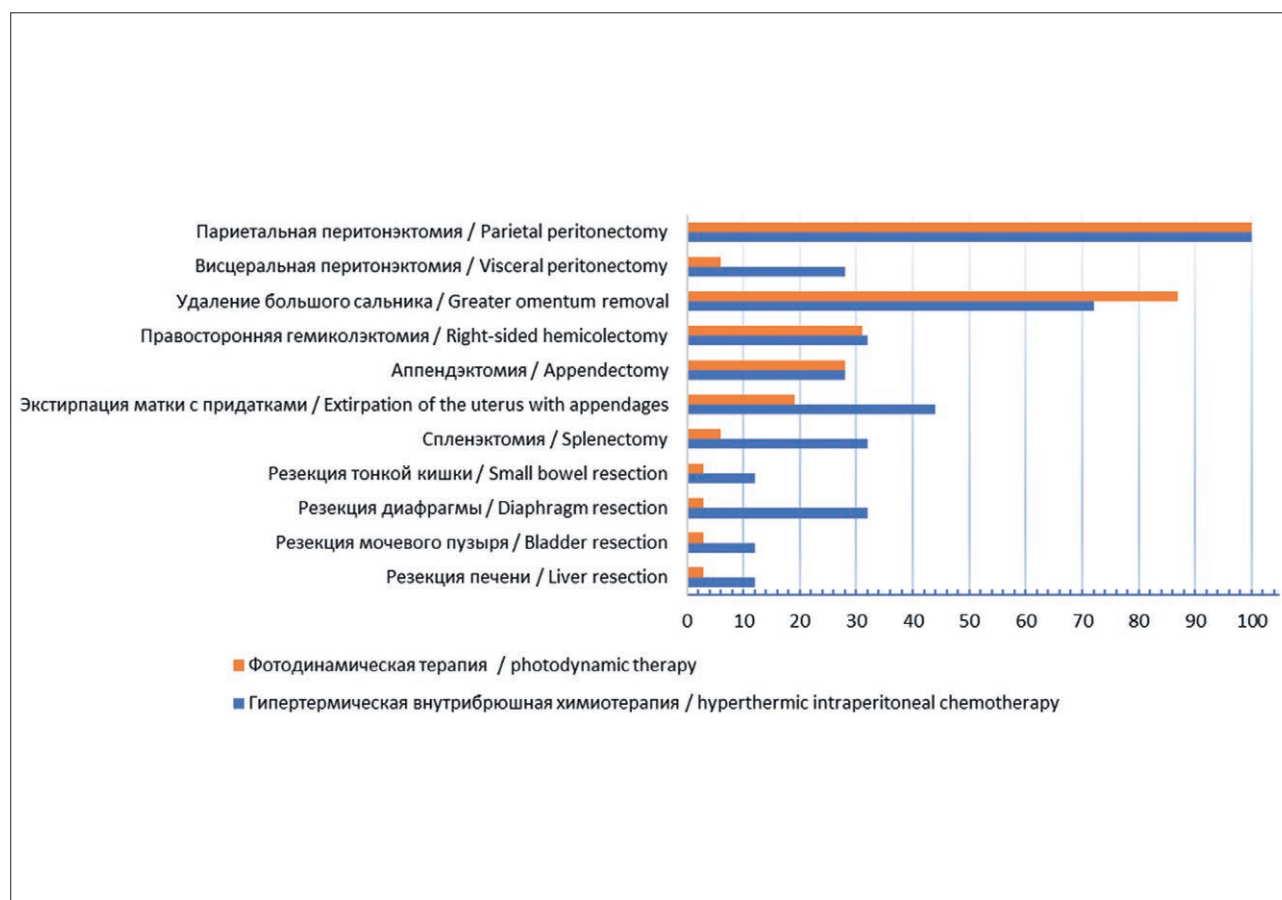


Рис. 3. Распределение больных по объему операции
Fig. 3. Distribution of patients by volume of surgery

Results

Immediate results

The average PCI value in the general group of patients was 20.75 ± 10.6 . In the group which underwent IOFDT, it was higher, 22 ± 10.5 points, whereas in the HIPEC group it was 19.0 ± 8.9 points. A comparative assessment by the Mann-Whitney U-test revealed no significant difference in the prevalence of the process ($p=0.171$) (Fig. 1).

The quality of the operation was evaluated by the Complete Cyto-reduction Score. Optimal cyto-reduction (CC0-1) was achieved in 40 patients (70.2%), and in the remaining 17 patients (29.8%), the residual tumor ranged from 2.5 mm to 2.5 cm or more. When analyzing the quality of surgery in patients with IOFDT, it was found that the number of patients with optimal and non-optimal (CC2-3) cyto-reduction is approximately equal: 18 (51.4%) and 17 (48.6%), respectively. A completely different ratio was obtained in the group which underwent HIPEC. Optimal cyto-reduction was achieved in 21 (91.3%) patients, in which 18 (85.7%) had no residual tumor visualized (CC0), and the rest of the patients had tumor dimensions not

exceeding 2.5 mm (CC1). Suboptimal cyto-reduction (CC2) was observed in only 4 patients (8.7%). A comparative assessment shows that a significantly higher number of optimal cyto-reduction ($p=0.002$) was obtained in the group with intraoperative HIPEC (Fig. 2).

A comparative analysis of the performed scopes of surgery in the studied groups was carried out. All patients underwent subtotal parietal peritonectomy. Partial removal of the visceral layer is almost 5 times more often performed in patients with HIPEC: 28% versus 6.3% in the group with IOFDT. If the number of resections or extirpations of the large and small omentum (72% and 87.5%), hemicolectomies (32% and 31.2%), and appendectomies (28% and 28.1%) in the compared groups is similar, a clear tendency is observed concerning the higher number of surgical interventions in HIPEC group for the extirpation of the uterus with appendages (44% vs. 18.7%), splenectomy (32% vs. 6.3%), resection of the diaphragm (32% vs. 3.1%), resection of the bladder, liver, and small intestine (12% vs. 3.1%) (Fig. 3).

Complications during treatment were detected in 9 (15.7%) patients, including 3 in the IOFDT group and 6 in the HIPEC group. The hospital mortality rate

was 5.2%, all the deaths were in the HIPEC group. The characteristics of postoperative complications justify the choice of cytoreductive surgery as a treatment method, its volume, and the combination of intraoperative antitumor method. In the general group with optimal cytoreduction, complications were observed in 14.6%, and with CC2–CC3 cytoreduction completeness, in 20.8%. However, in patients who underwent IOFDT and achieved optimal cytoreduction, the complication rate was 11.1%, whereas in the group with HIPEC, the complication rate was more than twice as high (23.8%).

The analysis of the severity of complications in the general group of patients showed that Clavien-Dindo grade 2 was observed in 4 cases (IOFDT=2, HIPEC=2), 3a in 2 cases (IOFDT=1, HIPEC=1), 4a in 4 cases (all HIPEC), 4b in 4 cases (all HIPEC) and death (grade 5) occurred in 3 patients (all HIPEC). The data take into account the combination of these complications in 9 patients. The most frequent complication was gastrostasis, which was registered in 6 patients and was obviously associated with the removal of the omentum completely replaced by the tumor. In 2 cases, suppuration of the postoperative wound and perforation of the small intestine were revealed. In the comparative analysis, the complication rate in the HIPEC group was 24%, and the IOFDT group, 9.4%. All 3 fatal cases occurred in the HIPEC group, where the mortality rate was 12%. The main cause of death was multiple organ failure, its triggers being different: ileo-transverso-anastomosis failure, pancreatic necrosis, and multiple prolonged perforations of the small intestine. The patients underwent repeated relaparotomies, but the lethal outcome was not avoided. It is noteworthy that their PCI was in the range of 20–24 points, but it was necessary to achieve optimal cytoreduction (CC1 in 2 cases, CC0 in 1 case) to perform HIPEC. There were no lethal outcomes in the group with IOFDT.

Long-term results

The overall 5-year survival rate of patients in the HIPEC group was 86.6%. The median survival rate in the group of patients who were administered photodynamic therapy as an additional intraoperative method was 66 months, and the 5-year survival rate was 65.2%.

Discussion

The gold standard of treatment for patients with peritoneum pseudomyxoma is considered to be cytoreductive surgery with HIPEC. 5-year survival rates range from 62 to 92.5%, with a complication rate of 25–54.8% and a mortality rate of 2–9% [9–11]. However, these are the results in a carefully selected group of patients. In the actual practice, when there are only a few centers providing surgical treatment of carcino-

matosis in Russia, and the number of patients, despite the extremely low incidence, is still high, we should not limit ourselves to considering the treatment tactics for such a small group. Another important point is the contraindications to the use of hyperthermic chemotherapy. General restrictions include age over 70, urinary system function issues, respiratory failure; local restrictions include the need to perform optimal cytoreduction. The penetration depth of the cytostatic agent, even at 42–43°C, is limited to 3 mm. Leaving a larger residual tumor, especially in the case of CC3, makes this very aggressive procedure useless. There are no approved standards for the treatment of patients with peritoneum pseudomyxoma, so a personalized treatment plan is selected for each patient. The surgery must be carefully planned. CT-PCI or ultrasound PCI is used to determine the prevalence of the process, the involvement of the serosa of the small and large intestine and their mesentery, the hepatoduodenal ligament, and the omentum sac. Based on the accumulated experience, we believe that with a PCI above 20 points it is not practical to plan cytoreduction with HIPEC, since an attempt to achieve optimal completeness of cytoreduction is not only questionable, but may also lead to the development of fatal complications. The use of IOFDT as an antitumor agent is limited by the need for exposure of the photosensitizer for 4 to 48 hours and the complexity of the effect on the visceral peritoneum. However, there are studies proving that the dose absorbed during the surgical stage of treatment from the operating theatre lamps, i. e., over at least 4 hours, corresponds to that of laser irradiation, and the treatment in this case is performed for both peritoneal layers [12]. In addition, the analysis of postoperative complications confirmed the safety of this technique and the fact that there are nearly no contraindications to its use. And the long-term results obtained, which take into account the initial PCI values and significantly worse cytoreduction indicators in the IOFDT group, make the IOFDT method more preferable in the clinical situation described due to the significantly lower frequency of post-operative complications and the absence of mortality.

Conclusion

The philosophy of treating patients with peritoneum pseudomyxoma involves maximum possible removal of tumor tissue from the abdominal cavity. Given the absence of hematogenic and lymphogenic metastasis in this disease, it is local control that determines the patient's prognosis and quality of life. The limited possibilities of systemic chemotherapy for mucinous neoplasia lead to surgical aggression and radicalism, however, the effectiveness of the

treatment depends on a careful choice of the happy middle ground based on a reasonable balance be-

tween the possible completeness of cytoreduction and the quality of life.

REFERENCES

1. Lord A.C., Shihab O., Chandrakumaran K., Mohamed F., Cecil T.D., Moran B.J. Recurrence and outcome after complete tumour removal and hyperthermic intraperitoneal chemotherapy in 512 patients with pseudomyxoma peritonei from perforated appendiceal mucinous tumours. *Eur J Surg Oncol*, 2015, vol. 41 (3), pp. 396–9. doi: 10.1016/j.ejso.2014.08.476.
2. Sparks D.S., Morris B., Xu W., Fulton J., Atkinson V., Meade B., Lutton N. Cytoreductive surgery and heated intraperitoneal chemotherapy for peritoneal carcinomatosis secondary to mucinous adenocarcinoma of the appendix. *Int Surg*, 2015, vol. 100 (1), pp. 21–8. doi: 10.9738/INTSURG-D-14-00089.1
3. Arnason T., Kamionek M., Yang M., Yantiss R.K., Misdraji J. Significance of proximal margin involvement in low-grade appendiceal mucinous neoplasms. *Arch Pathol Lab Med*, 2015, vol. 139 (4), pp. 518–521.
4. Overman M.J., Fournier K., Hu C.Y., Eng C., Taggart M., Royal R., Mansfield P., Chang G.J. Improving the AJCC/TNM staging for adenocarcinomas the appendix: the prognostic impact of histological grade. *Annals of surgery*, 2013, vol. 257 (6), pp. 1072–1078.
5. Grishin N.A., Suleimanov E.A., Lozhkin M.N., Chissov V.I., Urlova A.N., Shul'Gin M.A., Kaprin A.D., Filonenko E.V. Cytoreductive surgical treatment with intraoperative photodynamic therapy in patients with mucinous peritoneal carcinomatosis. *Biomedical Photonics*, 2017, Vol. 6 (3), pp. 49–52.
6. Sokolov V.V., Chissov V.I., Filonenko E.V., Zharkova, N.N., Kozlov, D.N., Smirnov V.V., Clinical fluorescence diagnostics in the course of photodynamic therapy of cancer with the photosensitizer PHOTOGEM. *Proceedings of SPIE – The International Society for Optical Engineering*, 1995, Vol. 2325, pp. 375–380.
7. Filonenko E.V. The history of development of fluorescence diagnosis and photodynamic therapy and their capabilities in oncology. *Russian Journal of General Chemistry*, 2015, Vol. 85 (1), pp. 211–216.
8. Sokolov V.V., Chissov V.I., Filonenko E.V., Yakubovskaya R.I., Sukhin D.G., Galpern M.G., Vorozhtsov G.N., Gulina A.V., Zhitkova, M.B., Zharkova, N.N., Kozlov D.N., Smirnov V.V. First clinical results with a new drug for PD. *Proceedings of SPIE – The International Society for Optical Engineering*, 1995, vol. 2325, pp. 364–366.
9. Robella M., Vaira M., Cinquegrana A., Borsano A., De Simone M. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy: risk factors for morbidity and postoperative outcome. *Minerva Chir*, 2019, vol. 74 (3), pp. 195–202. doi: 10.23736/S0026-4733.18.07649-6
10. Oemrawsingh A., de Boer N.L., Brandt-Kerkhof A.R.M., Verhoef C., Burger J.W.A., Madsen E.V.E. Short-term complications in elderly patients undergoing CRS and HIPEC: A single center's initial experience. *Eur J Surg Oncol*, 2019, vol. 45 (3), pp. 383–388. doi: 10.1016/j.ejso.2018.10.545
11. Rizvi S.A., Syed W., Shergill R. Approach to pseudomyxoma peritonei. *World J Gastrointest Surg*, 2018, vol. 10 (5), pp. 49–56. doi: 10.4240/wjgs.v10.i5.49
12. Suleimanov E.A. *Intraoperatsionnaya fluorestsennaya diagnostika i fotodinamicheskaya terapiya bol'nykh s pervichnymi i metastaticheskimi opukholyami bryushiny*. Avtoreferat dissertatsii na soiskanie uchenoj stepeni doktora med.nauk.

ЛИТЕРАТУРА

1. Lord A.C., Shihab O., Chandrakumaran K., Mohamed F., Cecil T.D., Moran B.J. Recurrence and outcome after complete tumour removal and hyperthermic intraperitoneal chemotherapy in 512 patients with pseudomyxoma peritonei from perforated appendiceal mucinous tumours. *Eur J Surg Oncol*. – 2015. – Vol. 41 (3). – P. 396–9. doi: 10.1016/j.ejso.2014.08.476.
2. Sparks D.S., Morris B., Xu W., Fulton J., Atkinson V., Meade B., Lutton N. Cytoreductive surgery and heated intraperitoneal chemotherapy for peritoneal carcinomatosis secondary to mucinous adenocarcinoma of the appendix. *Int Surg*. – 2015. – Vol. 100 (1). – P. 21–8. doi: 10.9738/INTSURG-D-14-00089.1
3. Arnason T., Kamionek M., Yang M., Yantiss R.K., Misdraji J. Significance of proximal margin involvement in low-grade appendiceal mucinous neoplasms. *Arch Pathol Lab Med*. – 2015. – Vol. 139 (4). – P. 518–521.
4. Overman M.J., Fournier K., Hu C.Y., Eng C., Taggart M., Royal R., Mansfield P., Chang G.J. Improving the AJCC/TNM staging for adenocarcinomas the appendix: the prognostic impact of histological grade. *Annals of surgery*. – 2013. – Vol. 257 (6). – P. 1072–1078.
5. Grishin N.A., Suleimanov E.A., Lozhkin M.N., Chissov V.I., Urlova A.N., Shul'Gin M.A., Kaprin A.D., Filonenko E.V. Cytoreductive surgical treatment with intraoperative photodynamic therapy in patients with mucinous peritoneal carcinomatosis. *Biomedical Photonics*. – 2017. – Vol. 6 (3). – P. 49–52.
6. Sokolov V.V., Chissov V.I., Filonenko E.V., Zharkova, N.N., Kozlov, D.N., Smirnov V.V., Clinical fluorescence diagnostics in the course of photodynamic therapy of cancer with the photosensitizer PHOTOGEM. *Proceedings of SPIE – The International Society for Optical Engineering*. – 1995. – Vol. 2325. – P. 375–380.
7. Filonenko E.V. The history of development of fluorescence diagnosis and photodynamic therapy and their capabilities in oncology. *Russian Journal of General Chemistry*. – 2015. – Vol. 85 (1). – P. 211–216.
8. Sokolov V.V., Chissov V.I., Filonenko E.V., Yakubovskaya R.I., Sukhin D.G., Galpern M.G., Vorozhtsov G.N., Gulina A.V., Zhitkova, M.B., Zharkova, N.N., Kozlov D.N., Smirnov V.V. First clinical results with a new drug for PD. *Proceedings of SPIE – The International Society for Optical Engineering*. – 1995. – Vol. 2325. – P. 364–366.
9. Robella M., Vaira M., Cinquegrana A., Borsano A., De Simone M. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy: risk factors for morbidity and postoperative outcome. *Minerva Chir*. – 2019. – Vol. 74 (3). – P. 195–202. doi: 10.23736/S0026-4733.18.07649-6
10. Oemrawsingh A., de Boer N.L., Brandt-Kerkhof A.R.M., Verhoef C., Burger J.W.A., Madsen E.V.E. Short-term complications in elderly patients undergoing CRS and HIPEC: A single center's initial experience. *Eur J Surg Oncol*. – 2019. – Vol. 45 (3). – P. 383–388. doi: 10.1016/j.ejso.2018.10.545
11. Rizvi S.A., Syed W., Shergill R. Approach to pseudomyxoma peritonei. *World J Gastrointest Surg*. – 2018. – Vol. 10 (5). – P. 49–56. doi: 10.4240/wjgs.v10.i5.49
12. Сулейманов Э.А. *Интраоперационная флуоресцентная диагностика и фотодинамическая терапия больных*

с первичными и метастатическими опухолями брюшины.
Автореферат диссертации на соискание ученой степени
доктора мед.наук. – Москва, 2017. – 48 с.

[Intraoperative fluorescence diagnostics and photodynamic
therapy of patients with primary and metastatic tumors of
the peritoneum. Abstract of dissertation for the degree of
Doctor of Medical Sciences]. Moscow, 2017. 48 p.