ORIGINAL ARTICLES

PALLIATIVE SURGICAL TREATMENT USING PHOTODYNAMIC THERAPY FOR BILIARY CANCER COMPLICATED BY OBSTRUCTIVE JAUNDICE

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Abstract

The article presents the results of a study of survival, markers of hemostasis, proteolysis, and tumor invasion after complex palliative treatment of patients with histologically verified malignant tumors of the bile ducts complicated by obstructive jaundice in two comparable groups of patients. The aim of the study was to evaluate the effectiveness of palliative surgical treatment using photodynamic therapy in patients with malignant tumors of the biliary system complicated by obstructive jaundice. In 10 patients of the main group, palliative surgical treatment was performed using photodynamic therapy; in 20 patients of the comparison group, palliative surgical treatment was performed without photodynamic therapy. In patients of the main group, a statistically significant increase in life expectancy by 104 days (p=0.033) was observed compared to the comparison group. At the same time, a statistically significant effect of tumor necrosis factor α, a marker of tumor invasion, on survival (p = 0.012) and a decrease in its level after photodynamic therapy by 15 pg/ml (p=0.041) was revealed. Thus, palliative treatment using photodynamic therapy of malignant tumors of the bile ducts, complicated by obstructive jaundice, can increase the survival rate of patients by reducing tumor invasion.

Key words: biliary cancer; photodynamic therapy; survival.

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ПАЛЛИАТИВНОЕ ХИРУРГИЧЕСКОЕ ЛЕЧЕНИЕ С ПРИМЕНЕНИЕМ ФОТОДИНАМИЧЕСКОЙ ТЕРАПИИ БОЛЬНЫХ СО ЗЛОКАЧЕСТВЕННЫМИ НОВООБРАЗОВАНИЯМИ ЖЕЛЧЕВЫВОДЯЩЕЙ СИСТЕМЫ, ОСЛОЖНЕННЫМИ ОБСТРУКТИВНОЙ ЖЕЛТУХОЙ

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Резюме

В работе представлены результаты исследования выживаемости, маркеров гемостаза, протеолиза и опухолевой инвазии после комплексного паллиативного лечения больных с гистологически верифицированными злокачественными новообразованиями желчевыводящих протоков, осложненными обструктивной желтухой в двух сопоставимых группах больных. Целью исследования было оценить эффективность паллиативного хирургического лечения с применением фотодинамической терапии (ФДТ) у больных злокачественными новообразованиями желчевыводящей системы, осложненными обструктивной желтухой. У 10 пациентов основной группы проводилось паллиативное хирургическое лечение с применением ФДТ, у 20 пациентов группы сравнения проводилось паллиативное хирургическое лечение без применения ФДТ. У пациентов основной группы наблюдалось статистически значимое увеличение продолжительности жизни по сравнению с группой сравнения на 104 дня (p=0,033). При этом выявлено статистически значимое влияние маркера опухолевой инвазии – фактора некроза опухоли α на выживаемость (p=0,012) и уменьшение его уровня после ФДТ с 43,53±33,99 пг/мл до 28,33±26,12 пг/мл (p = 0,041). Таким образом, паллиативное лечение с применением ФДТ злокачественных новообразований желчевыводящих протоков, осложненных обструктивной желтухой, позволяет увеличить выживаемость пациентов за счет уменьшения опухолевой инвазии.

Ключевые слова: злокачественные новообразования желчевыводящей системы, фотодинамическая терапия, выживаемость.

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Introduction

Biliary tract cancer is a rare oncological pathology, which includes distal and proximal cholangiocarcinoma, and gallbladder cancer [1, 2, 3]. The structure of morbidity and mortality in biliary cancer is assessed together with hepatocellular cancer [1]. The prevalence of cancer of the biliary tract together with hepatocellular cancer is 6.7 per 100,000 population. Malignant neoplasms of the bile ducts have one of the highest rates of overall mortality (35.2%) and mortality in the first year after diagnosis (66.8%) [1-5].

Despite the development of methods of radiation and chemotherapy, the main method of treatment of biliary cancer remains surgical. However, at the time of diagnosis, 57.3% of patients already have an advanced stage IV of the underlying disease, and 80.3% of patients have an advanced or locally advanced process [1, 2]. Thus, more than 80% of patients can only undergo palliative treatment, the main component of which is the elimination of life-threatening complications of the underlying disease, such as obstructive jaundice and cholangitis [4–6].

One of the methods of palliative treatment that complements surgical treatment is photodynamic therapy (PDT). PDT is a method of treating malignant neoplasms, in which the tumor is irradiated with light of a certain wavelength, which transfers the molecules of a special substance (a photosensitizer) selectively accumulated in the tumor tissue, into an excited state in the presence of oxygen. The resulting reactive oxygen species lead tumor cells to death by apoptosis, necrosis, and autophagy. Studies of the effectiveness of PDT in cancer of the biliary tract conducted in previous years gave encouraging results, indicating the promise of this method in the palliative treatment of this category of patients, which increases the survival of patients to an average of 8 months when local PDT is performed with hematoporphyrin derivatives [8-13].

The aim of the study was to evaluate the effectiveness of palliative surgical treatment using PDT in patients with malignant neoplasms of the biliary system complicated by obstructive jaundice.

Materials and Methods

An open non-randomized comparative survival study included 30 patients with histologically verified bile duct adenocarcinoma complicated by obstructive jaundice, who underwent complex treatment at the regional hepatological center of the City Hospital No. 5, Barnaul (Barnaul, Russia) from 2016 to 2020. The patients were divided into two groups. The inclusion criteria for the study were age over 18 years, histologically verified diagnosis of a malignant neoplasm of the bile ducts, and signed informed consent for surgical treatment during hospitalization. The exclusion criteria were mortality during the hospital stay and the presence of blood cancer. The main group included 10 patients who underwent palliative surgical treatment with PDT. The comparison group included 20 patients who underwent palliative surgical treatment without PDT. The distribution of patients into groups was carried out without the use of randomization. Patients who signed a consent to PDT due to the presence of contraindications to the use of alternative methods of treatment were included in the main group. Patients who refused PDT were included in the comparison group. The design of the study was approved by the Local Ethics Committee of the Altai State Medical University of the Ministry of Health of the Russian Federation (extract from protocol No. 11 dated November 27, 2017). Comparative characteristics of groups by sex, age, routine laboratory parameters of inflammation, bilirubinemia, and liver enzymes are presented in Table. 1. The groups were comparable in terms of the main characteristics.

Comparative characteristics of the groups according to the localization of the malignant neoplasm are presented in Table. 2. No statistically significant differences were found.

Palliative surgical treatment included surgical treatment of life-threatening complications, primarily of obstructive jaundice: percutaneous transhepatic mono- and bilobar drainage of the bile ducts, and bile duct stenting under ultrasound and X-ray control. Symptomatic conservative treatment included infusion, detoxification, analgesic, hepatoprotective, and antibacterial therapy [4, 5].

All patients of the main group underwent PDT according to the following algorithm: fluorescence diagnosis on a laser electron-spectrum device "Biospec" (New Surgical Technologies, Russia), local and systemic PDT on a programmed two-wavelength laser device "LAMI-Helios (LLC New Surgical technologies",

Таблица 1
Характеристика пациентов, включенных в исследование
Table 1
Characteristics of patients included in the study

Показатель Value	Основная группа Main group	Группа сравнения Comparison group	p
	M± SD	M± SD	
Возраст, лет Age, years	61,3±16,9	69,8±9,4	0,168
Число женщин Number of women	2	5	0,879
Число мужчин Number of men	8	15	0,879
Лейкоциты, *109/л Leukocytes, *109/L	8,87±3,16	9,71±2,16	0,487
Тромбоциты, *109/л Thrombocytes, *109/L	285,33±164,42	258,67±43,15	0,649
Общий билирубин, мкмоль/л Common bilirubin, mcmol/L	197,32±173,09	115,00±56,19	0,210
АСТ, Ед/л AST, U/L	96,83±63,07	53,17±29,51	0,097
АЛТ, Ед/л ALT, U/L	98,99±73,51	58,22±41,79	0,206

Примечание: p – статистическая значимость различий между основной группой и группой сравнения.
Note: p – statistical significance of differences between the main group and the comparison group.

Russia) according to TU 9444-001-53807582-2010. Photoditazine based on chlorin e6 (LLC VETA-GRAND, Russia) was used as a photosensitizer. Systemic PDT was performed through peripheral access to the cubital vein with monochromatic light with a wavelength of 662-665 nm with a light dose of 1200-1400 J/cm^2 with a power of 0.7 W and a radiation power density of 0.22 W/cm^2 using an apparatus for intravenous blood irradiation during intravenous administration of a photosensitizer at a dose of 1-1.4 mg/kg of body weight. Local contact PDT was carried out by irradiation with monochromatic light with a wavelength of 662 nm at a light dose of 220 J/cm^2 with a programmed specialized two-wavelength laser apparatus with a power of 0.7 W and a radiation power density of 0.22 W/cm^2 after 5 hours from the end of systemic PDT [6]. Access for PDT was carried out by percutaneous transhepatic external drainage of the bile ducts under ultrasound control. Then a conductor was inserted through the lumen of the common bile duct and brought down into the duodenum. The major duodenal papilla was cannulated along the retracted guidewire and endoscopic papillosphincterotomy was performed on the guidewire, after which endoscopic balloon dilatation of the lumen of the intramural part of the choledochus was performed along the guidewire and the introduction of the DPOC guiding catheter with its fixation. Then, a transnasal gastroscope was inserted through the DPOC catheter into the lumen of the choledochus. The balloon was inflated in the area of the bifurcation of the lobar ducts. Then, transluminal PDT was performed under video endoscopic visual control. The purpose of local PDT was to normalize the outflow through the extrahepatic bile ducts by reducing the volume of tumor tissue in the lumen of the bile ducts with the appearance of both fluoroscopically and visually free lumen (priority application notification and registration No. 2023105379).

Complications of surgical treatment were assessed using the Clavien-Dindo scale [14].

Determination of plasma fibrinogen concentration according to Clauss (1957) was carried out using a set of reagents from the Technology-Standard company (Russia).

To determine the concentration of tissue plasminogen activator (t-PA), tissue plasminogen activator inhibitor-1 (PAI-1), tissue factor (TF), tissue factor pathway inhibitor (TFPI), and tumor necrosis factor-alpha (TNF-α) in serum standard kits for enzyme immunoassay TECHNOZYM manufactured by Technoclone Herstellung von Diagnostika und Arzneimitteln GmbH (Austria) were used. Optical density was measured using a universal automatic photometer for microplates Elx808 from BioTec Instruments, Inc. (USA).

Statistical analysis was performed using the SigmaPlot 14.0 statistical software package (registration number 775400014). When testing normality using the Shapiro-Wilk test, it was revealed that all the studied indicators, except for gender and age, had a distribution that did not correspond to the Gaussian distribution in both groups. For the analysis of independent samples, the nonparametric Mann-Whitney test was used, and for paired samples, the Wilcoxon test was used. To compare unrelated groups with a normal distribution, the Student's parametric test was used, and for relative values – Fisher's z-test. The method of Kaplan-Meier curves was used to assess the overall life expectancy, and the log-rank test was used for a comparative analysis of survival. To assess the influence of factors on the prognosis of the disease, multiple linear regression analysis was used. The critical level of significance of the study results was taken as $p < 0.05$.

Таблица 2
Сравнительная характеристика больных по локализации и распространенности новообразования
Table 2
Comparative characteristics of patients by localization and prevalence of tumor

Локализация злокачественного новообразования Localisation of malignant tumor	Основная группа Main group		Группа сравнения Comparison group		p
	абс. abs.	%	абс. abs.	%	
Дистальная холангиокарцинома, в том числе Distal cholangiocarcinoma including	2	20,00	9	45,00	0,348
стадия IIIa по классификации TNM (8 редакция) stage IIIa according to the TNM classification (8th edition)	1	10,00	7	35,00	0,307
стадия IV по классификации TNM (8 редакция) stage IV stage according to TNM classification (8 edition)	1	10,00	2	10,00	0,519
Проксимальная холангиокарцинома, в том числе Proximal cholangiocarcinoma including	5	50,00	6	30,00	0,503
тип II по классификации Bismuth-Corlette Bismuth-Corlette type II	2	20,00	1	5,00	0,519
тип IIIa/IIIb по классификации Bismuth-Corlette Bismuth-Corlette type IIIa/IIIb	2	20,00	5	25,00	0,879
тип IV по классификации Bismuth-Corlette Bismuth-Corlette type IV	1	10,00	0	0,00	
стадия IIIa по классификации TNM (8 редакция) stage IIIa according to the TNM classification (8th edition)	2	20,00	5	25,00	0,879
стадия IV по классификации TNM (8 редакция) stage IV according to TNM classification (8 edition)	3	30,00	1	5,00	0,184
Аденокарцинома большого дуоденального сосочка, в том числе Adenocarcinoma of big duodemal ampulla including	3	30,00	3	15,00	0,628
стадия IIIa по классификации TNM (8 редакция) stage IIIa according to the TNM classification (8th edition)	2	20,00	2	10,00	0,849
стадия IV по классификации TNM (8 редакция) stage IV according to TNM classification (8 edition)	1	10,00	1	5,00	0,796
Желчный пузырь Gallbladder	0	0,00	2	10,00	0,796
стадия IV по классификации TNM (8 редакция) stage IV according to TNM classification (8 edition)	0	0,00	2	10,00	0,796

Примечание: p – статистическая значимость различий между основной группой и группой сравнения.
Note: p – statistical significance of differences between the main group and the comparison group.

Results and Discussion

In 1 patient (10.0%) of the main group, postoperative acute hemorrhagic anemia was observed after percutaneous transhepatic monolobar drainage of the bile ducts. Complications after PDT were not observed.

In 2 patients (10.0%) of the comparison group, prolapse of percutaneous transhepatic drainage with the development of bile peritonitis was detected, in 1 patient (5.0%) of the comparison group, postoperative acute hemorrhagic anemia was observed after percutaneous transhepatic monolobar drainage of the bile ducts. In a comparative analysis, the groups were comparable both in terms of the total number of postoperative complications (p=0.519) and in Clavien-Dindo stratification: 1 (10.0%) grade IIIa complications in the main group and 3 (15.0%) in the comparison group (p=0.849) [7].

When assessing life expectancy in parallel compared groups (Table 3), a statistically significantly higher median survival was found in the main group compared to the comparison group (p = 0.033) (Fig. 1).

At present, there are still few studies on palliative PDT for malignant neoplasms of the bile ducts, and the results of studies vary significantly [8-13]. In the studies of Haider et al. [8] the median survival of patients who underwent PDT was 14 months (9 patients with distal cholangiocarcinoma, local PDT with a photosensitizer based on a hematoporphyrin derivative at a dose of 2 mg/kg with monochromatic light irradiation with a

Таблица 3
Сравнительный анализ выживаемости больных
Table 3
Comparative analysis of survival of patients

Группа Group	Медиана выживания, дни Median survival, days Me (Q1; Q3)	95% доверительный интервал 95% confidence interval	p
Основная Main	170 (1648;113)	-25,235-365,235	0,033
Сравнения Comparison	66 (200;29)	33,13-98,87	

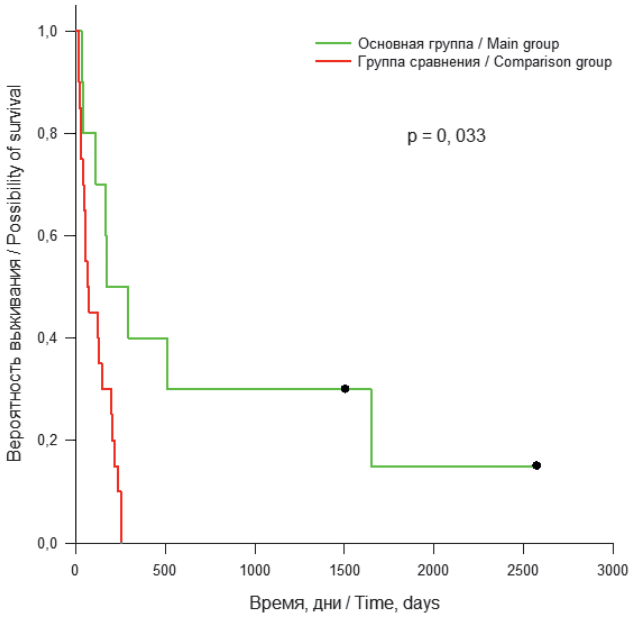

Рис. 1. Общая выживаемость пациентов основной группы и группы сравнения.
Fig. 1. Overall survival of patients in the main group and comparison group.

wavelength of 630 nm with a light dose of 180 J/ cm^2). At the same time, in a meta-analysis by Moole et al. [11] based on 9 studies of the effectiveness of local PDT with hematoporphyrin derivatives a median survival rate of 7.6 months was obtained in patients with unresectable cholangiocarcinoma after PDT. On the other hand, a study by Pereira et al. [12] conducted a comparative analysis between the group that received palliative choledochal stenting and chemotherapy and the group that received combined treatment consisting of PDT and chemotherapy. After reaching a median survival of 8.4 months, patients who did not undergo PDT lived longer (46 patients with distal and proximal cholangiocarcinoma, gallbladder cancer, local PDT with a hematoporphyrin derivative at a dose of 2 mg/kg with monochromatic light irradiation with a wavelength of 630 -635 nm with a light dose of 186 J/cm^2). A meta-analysis by Maswikiti et al. [13] based on 7 studies of the combined use of PDT with hematoporphyrin derivatives and chemotherapy provide other data that patients who received combined PDT and chemotherapy lived twice as long as patients who received these treatments separately. Significant differences in the results of studies are due to the high dependence of PDT results on the light dose, power, and control of the laser delivery to the tumor tissue. At the same time, the issue of the possibility of improving long-term outcomes in patients with unresectable cholangiocarcinoma, including through PDT, which is a safe method of treatment according to the world literature and our data, remains relevant.

The analysis of indicators of inflammation, hemostasis, and proteolysis in dynamics was carried out. There was a statistically significant decrease in TNF-α after PDT from 43.53±33.99 pg/ml to 28.33±26.12 pg/ml (p = 0.041) (Fig. 2).

TNF-α is known as a significant factor in neovasculogenesis, which is the main component of tumor invasion during carcinogenesis due to stimulation of cyclooxygenase-2 (COX-2) production [14, 15]. Many studies have shown a direct proportional relationship between the concentration of TNF-α and the growth rate of a malignant neoplasm, leading to a decrease in overall life expectancy [14, 15].

We confirmed the literature data in the course of multiple linear regression analysis of factors affecting survival in patients with biliary cancer. A statistically significant inversely proportional effect on survival of TNF-α concentration before treatment was obtained (Table 4).

Changes in the hemostasis system in cancer patients are one of the leading problems of modern oncology, while thrombotic complications are one of the leading causes of death in cancer patients [15].

The results obtained confirm the data of previous studies. PDT is a safe method of choice for palliative surgical treatment of patients with biliary cancer. This is especially relevant for patients with advanced stage IV of the disease, in whom PDT can significantly increase life expectancy in the absence of side effects from therapy.

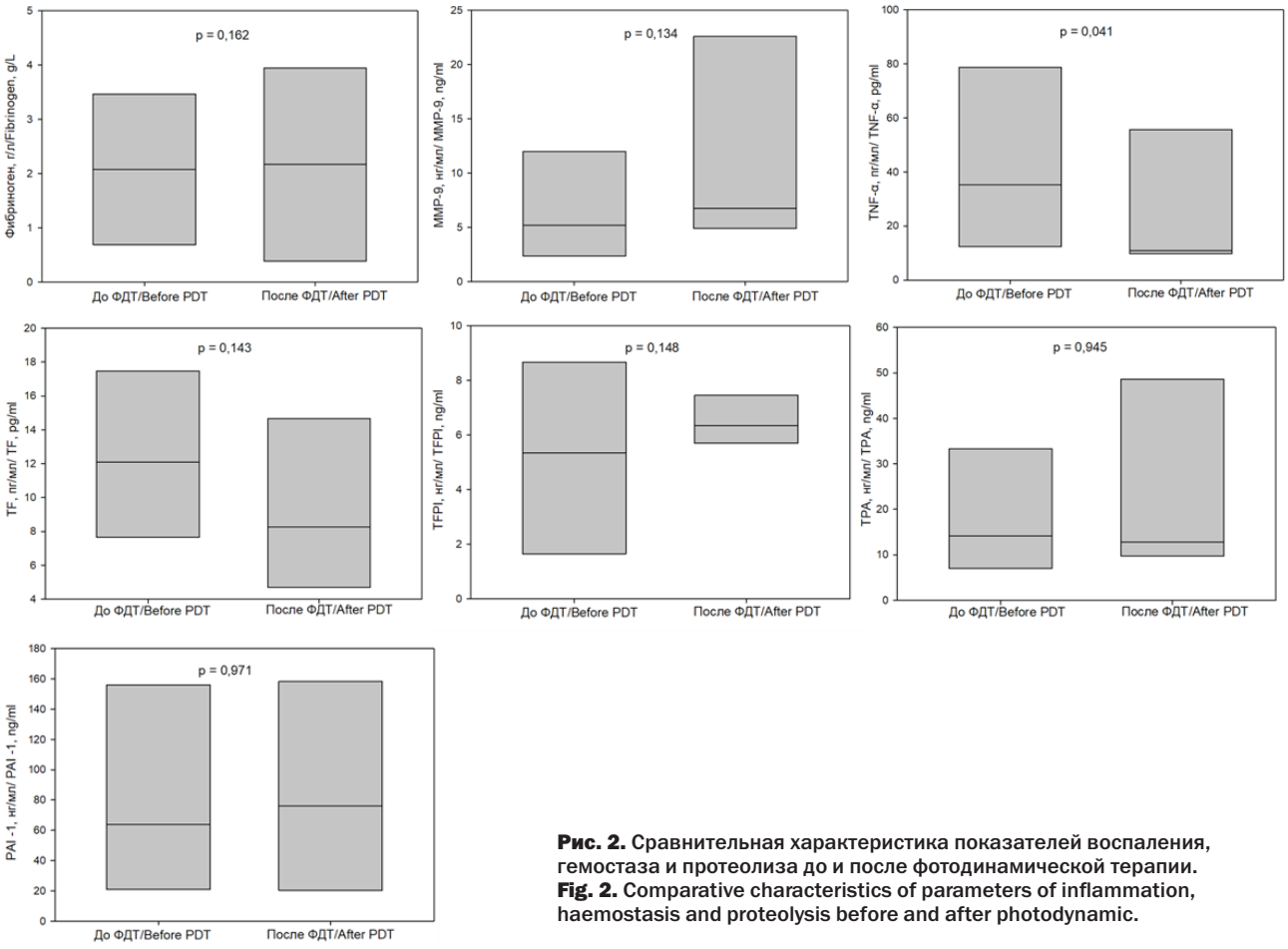

Рис. 2. Сравнительная характеристика показателей воспаления, гемостаза и протеолиза до и после фотодинамической терапии.
Fig. 2. Comparative characteristics of parameters of inflammation, haemostasis and proteolysis before and after photodynamic.

Таблица 4
Модель множественного линейного регрессионного анализа для оценки влияния значения TNF-α, TPA, PAI-1, общего билирубина до лечения на медиану выживаемости у пациентов основной группы

Table 4
Model of multiple linear regression analysis to assess the effect of TNF-α, TPA, PAI-1 and total bilirubin before treatment on the median survival in patients of the main group

Показатель Value	β±σ	p
Константа Constant	2003,485±393,260	<0,001
TNF-α	-17,074±5,659	0,012
TPA	-3,940±3,436	0,276
PAI-1	-3,525±2,721	0,222
Общий билирубин Common bilirubin	-1,260±1,021	0,243

Медиана выживаемости = 2003,485 – (17,074 * Показатель TNF- α) – (3,940 * Показатель TPA) – (3,525 * Показатель PAI-1) – (1,260 * Показатель общего билирубина)
Survival median = 2003,485 – (17,074 * Value of TNF- α) – (3,940 * Value of TPA) – (3,525 * Value of PAI-1) – (1,260 * Value of common bilirubin)

R =0,777; R2 =0,603; F =4,185; p =0,027

Conclusion

Thus, complex palliative treatment using PDT of malignant neoplasms of the bile ducts can increase the life expectancy of patients, while not having significant side effects on the patient. PDT may be recommended for the palliative treatment of biliary cancer.

REFERENCES

1. Status of oncological care for the population of Russia in 2020 / ed. A.D. Kaprin, V.V. Starinskogo, G.V. Petrova – *M .: MSIOI named after. P.A. Herzen, branch of the FSBI «NMICR» of the Russian Ministry of Health*, 2021, p. 239.
2. Zhang X. et al. Comparison of current guidelines and consensus on the management of patients with cholangiocarcinoma: 2022 update. *Intractable Rare Dis Res*, 2022, vol. 11(4), pp. 161-172.
3. Russian Oncology Association. Biliary cancer. Clinical guidelines. 2020. 51 p. Accessed March 23, 2023 (In Russian) https://oncology-association.ru/wp-content/uploads/2020/09/biliarnyj_rak.pdf
4. Zerem E., Imširović B., Kunosić S. et al. Percutaneous biliary drainage for obstructive jaundice in patients with inoperable, malignant biliary obstruction. *Clin Exp Hepatol*, 2022, vol. 8(1), pp. 70-77.
5. Shah R., John S. Cholestatic Jaundice. *In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing*, 2022, PMID: 29489239.
6. Tseimakh A.E. et al. Method for complex mini-invasive treatment of obstructive jaundice, cholangitis, intrahepatic abscesses of tumor genesis using local and systemic photodynamic therapy. Patent RF, no. 2704474, 2019. (In Russian)
7. Dindo D., Demartines N., Clavien P.A. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Annals of Surgery*, 2004, vol. 240(2), pp. 205-213.
8. Haider H., Chapman C.G., Siddiqui U.D. Maximizing survival in hilar cholangiocarcinoma patients using multi-modality therapy: photodynamic therapy (pdt) with stenting, chemotherapy, and radiation. *Gastrointestinal Endoscopy*, 2020, vol. 91(6), pp. 1-5. doi: 10.1016/j.gie.2020.03.2226
9. Lu Y. et al. Efficacy and safety of photodynamic therapy for unresectable cholangiocarcinoma: A meta-analysis. *Clinics and research in hepatology and gastroenterology*, 2015, vol. 39(6), pp. 718-724. doi: 10.1016/j.clinre.2014.10.015.
10. Li Z. et al. Long-Term Results of ERCP- or PTCS-Directed Photodynamic Therapy for Unresectable Hilar Cholangiocarcinoma. *Surg Endosc*, 2021, vol. 35(10), p p. 5655-5664. doi: 10.1007/s00464-020-08095-1
11. Moole H. et al. Success of Photodynamic Therapy in Palliating Patients With Nonresectable Cholangiocarcinoma: A Systematic Review and Meta-Analysis. *World J Gastroenterol*, 2017, vol. 23(7), pp. 1278–88. doi: 10.3748/wjg.v23.i7.1278
12. Pereira S.P. et al. PHOTOSTENT-02: Porfimer Sodium Photodynamic Therapy Plus Stenting Versus Stenting Alone in Patients With Locally Advanced or Metastatic Biliary Tract Cancer. *ESMO Open*, 2018, vol. 3(5), p. e000379. doi: 10.1136/esmoopen-2018-000379
13. Maswikiti E.P., Chen H. Photodynamic therapy combined with systemic chemotherapy for unresectable extrahepatic cholangiocarcinoma: A systematic review and meta-analysis. *Photodiagnosis Photodyn Ther*, 2023, vol 2 (41), p.103318. doi: 10.1016/j.pdpdt.2023.103318.
14. Момот А.П., Цывкина Л.П., Тараненко И.А. Современные методы распознавания состояния тромботической готовности. *Москва: Издательство «Знание-М»*, 2022, p. 146.
15. Streiff M.B. et al. Cancer-Associated Venous Thromboembolic Disease, Version 2.2021 NCCN Clinical Practice Guidelines in Oncology. *Journal of the National Comprehensive Cancer Network*, 2021, vol. 19(10), pp. 1181-1201.

ЛИТЕРАТУРА

1. Состояние онкологической помощи населению России в 2020 году / под ред. А.Д. Каприна, В. В. Старинского, Г. В. Петровой – М.: МНИОИ им. П.А. Герцена – филиал ФГБУ «НМИРЦ» Минздрава России. – 2021. – С. 239.
2. Zhang X. et al. Comparison of current guidelines and consensus on the management of patients with cholangiocarcinoma: 2022 update // Intractable Rare Dis Res. – 2022. – Vol. 11(4). – P. 161-172.
3. Общероссийский национальный союз «Ассоциация онкологов России». Рак желчевыводящей системы. Клинические рекомендации. – 2020. – С. 51. Ссылка активна на 23.03.2023. https://oncology-association.ru/wp-content/uploads/2020/09/biliarnyj_rak.pdf
4. Zerem E., Imširović B., Kunosić S. et al. Percutaneous biliary drainage for obstructive jaundice in patients with inoperable, malignant biliary obstruction // Clin Exp Hepatol. – 2022. – №8(1). – P. 70-77.
5. Shah R., John S. Cholestatic Jaundice // In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. – 2022. – PMID: 29489239.
6. Цеймах А.Е., Лазарев А.Ф., Куртуков В.А. и соавт. Способ комплексного мини-инвазивного лечения механической желтухи, холангита, внутрипеченочных абсцессов опухолевого генеза с применением локальной и системной фотодинамической терапии. – Патент РФ №2704474. – 2019. [Tseimakh A.E et al. Method for complex mini-invasive treatment of obstructive jaundice, cholangitis, intrahepatic abscesses of tumor genesis using local and systemic photodynamic therapy. Patent RF, no. 2704474. – 2019. (In Russian)]
7. Dindo D., Demartines N., Clavien P.A. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey // Annals of Surgery. – 2004. – Vol. 240(2). – P. 205-213.
8. Haider H., Chapman C.G., Siddiqui U.D. Maximizing survival in hilar cholangiocarcinoma patients using multi-modality therapy: photodynamic therapy (pdt) with stenting, chemotherapy, and radiation // Gastrointestinal Endoscopy. – 2020. – Vol. 91(6). – P. 1-5. doi: 10.1016/j.gie.2020.03.2226
9. Lu Y. et al. Efficacy and safety of photodynamic therapy for unresectable cholangiocarcinoma: A meta-analysis // Clinics and research in hepatology and gastroenterology. – 2015. – Vol. 39(6). – P. 718-724. doi: 10.1016/j.clinre.2014.10.015.
10. Li Z. et al. Long-Term Results of ERCP- or PTCS-Directed Photodynamic Therapy for Unresectable Hilar Cholangiocarcinoma // Surg Endosc. – 2021. – Vol. 35(10). – P. 5655-64. doi: 10.1007/s00464-020-08095-1
11. Moole H. et al. Success of Photodynamic Therapy in Palliating Patients With Nonresectable Cholangiocarcinoma: A Systematic Review and Meta-Analysis // World J Gastroenterol. – 2017. – Vol. 23(7). – P. 1278-88. doi: 10.3748/wjg.v23.i7.1278
12. Pereira S.P. et al. PHOTOSTENT-02: Porfimer Sodium Photodynamic Therapy Plus Stenting Versus Stenting Alone in Patients With Locally Advanced or Metastatic Biliary Tract Cancer // ESMO Open. – 2018. – Vol. 3(5). – P. e000379. doi: 10.1136/esmoopen-2018-000379
13. Maswikiti E.P., Chen H. Photodynamic therapy combined with systemic chemotherapy for unresectable extrahepatic cholangiocarcinoma: A systematic review and meta-analysis // Photodiagnosis Photodyn Ther. – 2023. – Vol. 2 (41). – P. 103318. doi: 10.1016/j.pdpdt.2023.103318.
14. А. П. Момот, Л. П. Цывкина, И. А. Тараненко Современные методы распознавания состояния тромботической готовности // Москва: Издательство «Знание-М». – 2022. – С. 146.
15. Streiff M.B. et al. Cancer-Associated Venous Thromboembolic Disease, Version 2.2021 NCCN Clinical Practice Guidelines in Oncology // Journal of the National Comprehensive Cancer Network. – 2021. – Vol. 19(10). – P. 1181-1201.