EFFECTIVENESS OF PALLIATIVE PHOTODYNAMIC THERAPY FOR UNRESECTABLE BILIARY CANCER. SYSTEMATIC REVIEW AND META-ANALYSIS

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Abstract

A systematic review and meta-analysis was aimed to assess the effectiveness of palliative photodynamic therapy for unresectable malignant tumors of the biliary system in order to justify the feasibility of including photodynamic therapy (PDT) in the complex treatment of this category of patients. Publications in the databases PubMed Central, the bibliographic database of scientific citations of the RSCI, and the Cochrane library were considered. Heterogeneity was assessed graphically using forest plots and statistically using tau^2 and I^2 statistics. A meta-analysis of 5-year survival revealed a statistically significantly longer pooled estimate of the survival period in groups where PDT was used – 339±161 days (95% CI 25-710; $p < 0.001$) compared to groups where PDT was not used – 83±16 days (95% CI 33-100; $p < 0.001$). Heterogeneity among studies was found to be statistically insignificant ($I^2 = 29\%$, $p = 0.23$). A meta-analysis of the risk difference for adverse events revealed a statistically significantly lower risk (-0.2306; 95% CI -0.3917-0.0696; $p = 0.005$) of adverse events after PDT compared with the comparison group. Heterogeneity among studies was found to be statistically insignificant ($I^2 = 0\%$, $p = 0.35$). There were no significant publication biases in either meta-analysis. The presented meta-analysis demonstrated that PDT may be the method of choice in the palliative complex treatment of patients with unresectable cholangiocarcinomas, increasing the five-year survival of patients along with the absence of increased risks of postoperative complications in comparison with other methods of palliative surgical treatment.

Key words: cholangiocarcinoma, photodynamic therapy, meta-analysis.

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ЭФФЕКТИВНОСТЬ ПАЛЛИАТИВНОЙ ФОТОДИНАМИЧЕСКОЙ ТЕРАПИИ У ПАЦИЕНТОВ С НЕРЕЗЕКТАБЕЛЬНЫМИ ЗЛОКАЧЕСТВЕННЫМИ НОВООБРАЗОВАНИЯМИ ЖЕЛЧЕВЫВОДЯЩЕЙ СИСТЕМЫ. СИСТЕМАТИЧЕСКИЙ ОБЗОР И МЕТААНАЛИЗ

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Резюме

Систематический обзор и метаанализ направлены на оценку эффективности паллиативной фотодинамической терапии (ФДТ) у пациентов с нерезектабельнысм злокачественными новообразованиями желчевыводящей системы с целью обоснования целесообразности включения ФДТ в комплексное лечение данной категории пациентов. Рассмотрены публикации в базах PubMed Central, библиографической базе данных научного цитирования РИНЦ, библиотеке Cochrane. Гетерогенность оценивали графически, используя лесные диаграммы, и статистически, используя статистику tau^2 и I^2. Метаанализ пятилетней выживаемости выявил статистически значимо большую общую выживаемость при объединенной оценке в группах, где применяли ФДТ – 339±161 дней (95% ДИ 25-710; $p < 0{,}001$) по сравнению с группами, где ФДТ не применяли – 83±16 дней (95% ДИ 33-100; $p < 0{,}001$). Гетерогенность исследований была признана статистически незначимой ($I^2 = 29\%$, $p = 0{,}23$). Метаанализ разницы рисков нежелательных явлений выявил статисти-

чески значимо меньший риск (-0,2306; 95% ДИ -0,3917-0,0696; p = 0,005) нежелательных явлений после ФДТ по сравнению с группой сравнения. Гетерогенность исследований была признана статистически незначимой (I^2 = 0%, p = 0,35). Значимых публикационных ошибок и предвзятости в обоих метанализах выявлено не было. Представленный метаанализ продемонстрировал, что ФДТ может быть методом выбора при паллиативном комплексном лечении пациентов с нерезектабельными злокачественными новообразованиями желчевыводящих протоков, увеличивающим пятилетнюю выживаемость пациентов наряду с отсутствием повышенных рисков послеоперационных осложнений в сравнении с другими методами паллиативного хирургического лечения.

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

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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 incidence and mortality in biliary cancer is assessed together with hepatocellular cancer [1]. Being one of the rarest oncological pathologies, assessed together with hepatocellular cancer with a prevalence of only 6.7 cases per 100 thousand population, malignant neoplasms of the bile ducts have one of the highest overall mortality (35.2%) and mortality in the first year from the date of diagnosis (66.8%) [1, 2, 3, 4, 5].

Despite the development of radiation and chemotherapy methods, surgery remains the main method of treating biliary cancer. However, at the time of diagnosis, 57.3% of patients already have 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, 5, 6].

One of the methods of palliative treatment that complements surgical treatment is photodynamic therapy (PDT). PDT is a method of treating malignant neoplasms, which involves irradiating the tumor with light of a certain wavelength, which causes molecules of a special substance, a photosensitizer, selectively accumulated in the tumor tissue, to an excited state in the presence of oxygen. The resulting active oxygen species cause tumor cells to die through apoptosis, necrosis, and autophagy. The first successful application of PDT in the palliative treatment of biliary tract cancer was a clinical example published by McCaughan et al. [7], which began the study of the effect of PDT on malignant neoplasms of the bile ducts. Conducted in 2015-2023 years studies of the effectiveness of PDT in biliary tract cancer have yielded encouraging results, indicating the promise of the PDT method in palliative treatment of this category of patients [8, 9, 10, 11, 12, 13]. The main advantages of PDT include its safety and the absence of side effects compared to chemotherapeutic treatment methods in the presence of a therapeutic effect that exceeds the results of treatment without PDT.

This systematic review and meta-analysis are aimed at assessing the effectiveness of palliative PDT in patients with unresectable malignant neoplasms of the biliary system in order to substantiate the feasibility of including PDT in the complex treatment of this category of patients. To achieve the goal set during the preparation of the systematic review and meta-analysis, it was necessary to solve the following problems:

1) to evaluate the safety of PDT in palliative treatment of patients with unresectable malignant neoplasms of the biliary system;
2) to evaluate five-year survival after the use of palliative PDT in patients with unresectable malignant neoplasms of the biliary system.

Materials and Methods

The systematic review was conducted in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [15]. For inclusion in the systematic review, we reviewed open-source publications in Russian and English in the PubMed Central database (Internet address: https://www.ncbi.nlm.nih.gov/pmc/), the bibliographic database of scientific citations RSCI (Internet resource: e-library.ru), and the Cochrane Library (Internet address: https://www.cochranelibrary.com/). The search for articles in these databases was conducted using the following keywords: photodynamic therapy, cholangiocarcinoma. The search strategy included identifying full-text articles presenting the materials and results of clinical studies. The titles, abstracts, and full texts of potentially eligible articles were independently reviewed by two researchers. Disagreements were resolved by a third investigator.

At the identification stage, 422 published full-text articles published between March 1998 and January 2024 were selected (Fig. 1). At the screening stage, 395

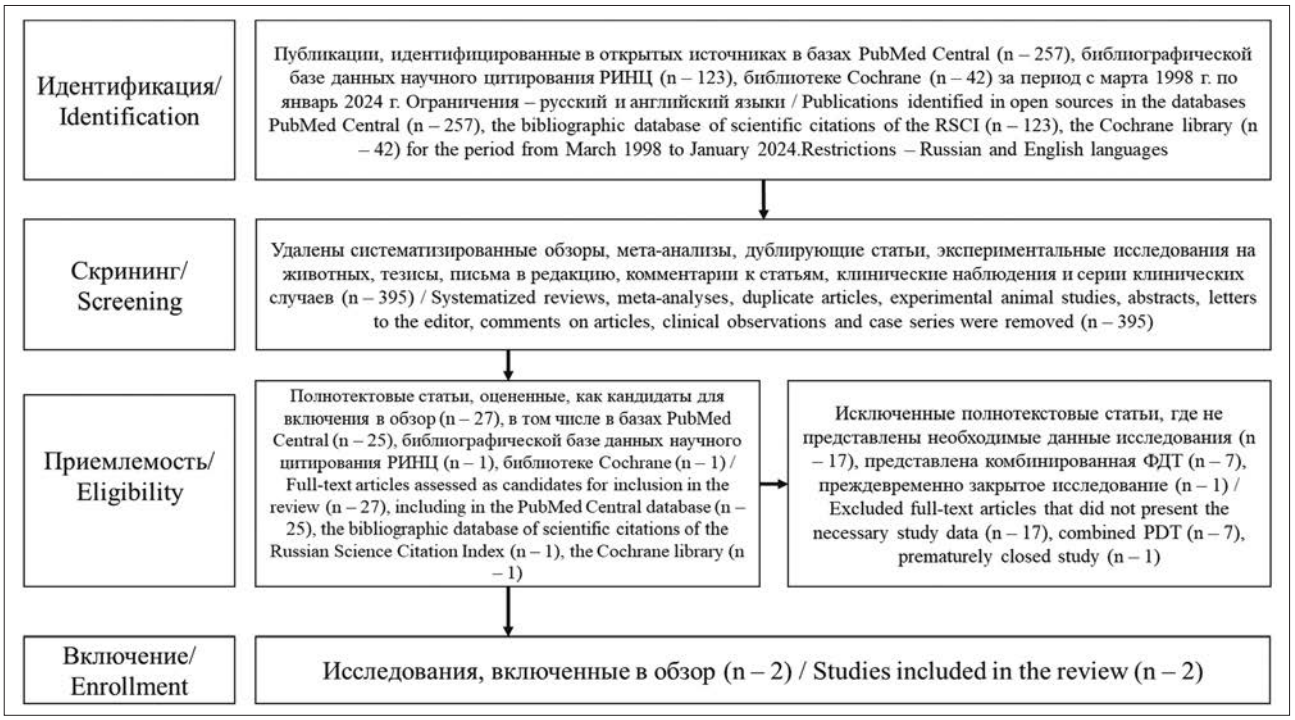

Рис. 1. Схема проведения систематического обзора и метаанализа в соответствии с рекомендациями PRISMA [15].
Fig. 1. Scheme for conducting a systematic review and meta-analysis according to PRISMA guidelines [15].

publications were excluded: systematic reviews, meta-analyses, duplicate articles, experimental animal studies, abstracts, letters to the editor, comments on articles, clinical observations and clinical case series were removed. As a result of multi-stage selection, 27 scientific publications were included.

Published studies that met the following inclusion criteria were considered eligible:

1) the study assessed the efficacy of PDT in the palliative treatment of unresectable cholangiocarcinoma in the adjuvant setting. Studies of PDT in the neoadjuvant setting or in patients with resectable cholangiocarcinoma were excluded;
2) the study assessed the efficacy of PDT monotherapy. Studies of the combined effects of PDT and other modalities such as chemotherapy and radiotherapy without PDT monotherapy were excluded;
3) the study provided sufficient data to assess 5-year survival, analyze adverse events according to the meta-analysis methodology, assess the risk of systematic errors, and describe all parameters of the PDT.

At the stage of assessing the eligibility criteria, 25 articles were excluded, including 17 publications due to missing data (recruitment to the studies was not completed, adverse events were not specified, five-year survival was not controlled, the full study design was not presented); 7 publications – in connection with the study of PDT in combination with chemotherapy and/or other radiation exposure; 1 study – due to premature closure of the study and the impossibility of correct calculation of five-year survival. Thus, 2 scientific publications were analyzed in a systematic review and meta-analysis.

When assessing the methodological quality of the studies, an analysis of the design's compliance with the study objectives, an assessment of the correctness of the statistical analysis and its compliance with the study design, and an assessment of the risk of systematic errors in the study were performed. The risk of systematic errors (bias of results) in randomized studies was assessed using the adapted and validated Russian version of the Cochrane Collaboration questionnaire [16]. The risk of systematic errors in non-randomized comparative case-control studies was analyzed using the corresponding Newcastle-Ottawa questionnaires [17].

Statistical analysis was performed using the Sigma Plot software package, version 14.0 (Registration number 775400014), the meta-analysis was performed with the additional use of the Cochrane RevMan Web Version: 7.5.0 graphical editor. The proportions of individual studies with survival rates (in days) and adverse events were combined using the double arcsine transformation (Freeman-Tukey transformation). Heterogeneity was assessed graphically using forest plots and statistically using tau^2 and I^2 statistics.

A fixed effects model was used because heterogeneity was not statistically significant. The tau^2 statistic reflects the degree of variation in prevalence observed across studies. An I^2 of 0%–39% was considered statistically insignificant heterogeneity, 40–75% as moderate heterogeneity, and 76%–100% as significant hetero-

geneity among the compared studies. A p-value ≥ 0.05 was taken to reject the null hypothesis that the studies are heterogeneous. Publication effect and selection bias in pooled estimates were tested using the Begg and Mazumdar test. Publication bias was assessed by constructing funnel plots. A p-value < 0.05 was taken to be statistically significant to support the null hypothesis.

Results

All studies that met the selection criteria were comparative prospective. Of the two studies included in the systematic review and meta-analysis, one was randomized and one was a cohort non-randomized study. When assessing the risk of systematic errors, all studies were characterized by high methodological quality (Table 1). All studies were characterized by adequate methods of statistical processing of research results in accordance with the objectives and design of their implementation.

The characteristics of PDT methods in the studies included in the systematic review and meta-analysis are presented in Table 2.

In the study by Tseimakh A.E. *et al.* (2023), the efficacy of intraluminal local and systemic PDT in patients with unresectable malignant neoplasms of the biliary tract was studied. The main group included 5 patients with stage III and 5 patients with stage IV according to the TNM classification. Of these, 5 patients had proximal cholangiocarcinoma: 2 patients – of type II, 2 patients – of type IIIa/IIIb, and 1 patient – of type IV according to the Bismuth-Corlette classification. The comparison group included 14 patients with stage III and 6 patients with stage IV according to the TNM classification. Of these, 6 patients had proximal cholangiocarcinoma: 1 patient –

Таблица 1
Оценка риска систематических ошибок в исследованиях эффективности исследований эффективности ФДТ нерезектабельных злокачественных новообразований желчевыводящей системы

Table 1
Assessing the risk of bias in efficacy studies of PDT efficacy studies of unresectable biliary tumors

Критерий риска систематической ошибки (оценка в баллах) в когортных нерандомизированных исследованиях [17] / Risk of bias criterion (score) in non-randomized cohort studies [17]	Цеймах А.Е. и др. (2023) / Tseimakh A.E. and others (2023)	Критерий риска систематической ошибки (оценка в баллах) в рандомизированных исследованиях [16] / Risk of bias criterion (score) in randomized trials [16]	Ortner M.E.J. et al. (2003)
Является ли экспонированная когорта репрезентативной? / Is the exposed cohort representative?	1	Метод рандомизации (систематическая ошибка распределения пациентов по группам) / Randomization method (systematic error in the distribution of patients into groups)	Низкий риск / Low risk
Каким образом была сформирована неэкспонированная когорта? / How was the unexposed cohort formed?	1	Сокрытие рандомизационной последовательности (систематическая ошибка распределения пациентов по группам) / Concealment of the randomization sequence (systematic error in the allocation of patients to groups)	Низкий риск / Low risk
Каким образом был установлен факт воздействия изучаемого фактора? / How was the fact of the influence of the studied factor established?	1	«Ослепление» пациентов и медперсонала (маскирование/сокрытие вмешательства от пациентов и медперсонала) в процессе лечения (систематическая ошибка исполнения; может оцениваться отдельно от каждого исхода) / Blinding of patients and staff (masking/concealing the intervention from patients and staff) during treatment (performance bias; may be assessed separately for each outcome)	Низкий риск / Low risk
Было ли подтверждено отсутствие интересующего исхода в начале исследования? / Was the absence of the outcome of interest confirmed at baseline?	1		
Являются ли сравниваемые когорты сопоставимыми? / Are the comparing cohorts comparable?	1	Пропуски в данных об исходах (систематическая ошибка пропуска данных; может оцениваться отдельно для каждого исхода) / Missing outcome data (missing data bias; may be assessed separately for each outcome)	Низкий риск / Low risk
Какой источник информации об исходах использовался? / What source of outcome information was used?	1	Представление результатов исследования (систематическая ошибка представления результатов исследования) / Presentation of research results (systematic error in the presentation of research results)	Низкий риск / Low risk

Была ли продолжительность наблюдения достаточной для возникновения интересующих исходов? / Was the duration of follow-up sufficient for the outcomes of interest to occur?	1	Другие возможные источники систематических ошибок / Other possible sources of systematic errors	Низкий риск / Low risk
Каково было выбывание пациентов? / What was the patient attrition rate?	1	Дополнительный источник систематических ошибок: конфликт интересов / Additional source of bias: conflict of interest	Неопределенный риск / Uncertain risk
Общая оценка методологического качества / Overall assessment of methodological quality	Высокое / High	Общая оценка методологического качества / Overall assessment of methodological quality	Высокое / High
Высокое методологическое качество – 8-9 баллов / High methodological quality – 8-9 points		Высокое методологическое качество, при низком риске всех ошибок или неопределенном риске одной систематической ошибки / High methodological quality, with low risk of all biases or uncertain risk of one bias	
Удовлетворительное методологическое качество – 6-7 баллов / Satisfactory methodological quality – 6-7 points		Удовлетворительное методологическое качество, при неопределенном риске двух и более систематических ошибок / Satisfactory methodological quality, with an uncertain risk of two or more systematic errors	
Низкое методологическое качество – 0-5 баллов / Low methodological quality – 0-5 points		Низкое методологическое качество, при высоком риске одной и более систематической ошибки / Low methodological quality, with a high risk of one or more systematic errors	

Таблица 2
Характеристика исследований эффективности ФДТ нерезектабельных злокачественных новообразований желчевыводящей системы, включенных в систематический обзор и метаанализ

Table 2
Characteristics of studies on the effectiveness of PDT for unresectable malignant tumors of the biliary system included in the systematic review and meta-analysis

Исследование/Дизайн/ Study/Design	Доза фотосенсибилизатора и техника ФДТ/ Photosensitizers dose and PDT technique	Выживаемость основной группы/группы сравнения и нежелательные явления основной группы/группы сравнения/ Survival of main/comparison group and adverse events of main/comparison group
1. Цеймах А.Е. и др. (2023) [18] / Открытое нерандомизированное сравнительное / 1. Tseimakh A.E. et al. (2023) [18] / Open non-randomized comparative	Фотодитазин 1-1,4 мг/кг за 5 ч до экспозиции с длиной волны 662 нм с экспозиционной дозой света 220 Дж/см^2, плотностью мощности излучения 0,22 Вт/см^2 / Photoditazine 1-1.4 mg/kg 5 hours before exposure to a wavelength of 662 nm with an exposure light dose of 220 J/cm^2, radiation power density 0.22 W/cm^2	170±100 (95% ДИ/CI 25-365)/ 66±17 (95% ДИ/CI 33-99) p < 0,05 1/3
2. Ortner M.E.J. et al. (2003) [19] / Открытое рандомизированное сравнительное / 2. Ortner M.E.J. et al. (2003) [19] / Open randomized comparative	Фотофрин 2 мг/кг за 48 ч до экспозиции с длиной волны 630 нм с экспозиционной дозой света 180 Дж/см^2, плотностью мощности излучения 0,24 Вт/см^2 / Photofrin 2 mg/kg 48 hours before exposure to a wavelength of 630 nm with an exposure light dose of 180 J/cm^2, radiation power density 0.24 W/cm^2	493±217 (95% ДИ/CI 276-710)/ 98±15 днями (95% ДИ/CI 83-100) p < 0,001 9/13 Серьезные нежелательные явления: 2 случая холангита, осложненного сепсисом. / Serious adverse events: 2 cases of cholangitis complicated by sepsis.

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.

of type II and 5 patients – of type IIIa/IIIb according to the Bismuth-Corlette classification. A statistically significant increase in survival was found in patients who received PDT with a median overall survival of 170±100 days (95% CI 25-365; p < 0.05) compared to the comparison group that did not receive PDT with a median overall survival of 66±17 days (95% CI 33-99; p < 0.05). No adverse events associated with PDT were identified [18]. One patient had acute posthemorrhagic anemia after percutaneous transhepatic monolobar drainage of the bile ducts

for mechanical jaundice. In the comparison group, 2 patients had loss of percutaneous transhepatic drainage with the development of bile peritonitis; 1 patient had postoperative acute hemorrhagic anemia after percutaneous transhepatic monolobar drainage of the bile ducts for mechanical jaundice [18].

In the study by Ortner M.E.J. et al. (2003), 20 patients with unresectable malignant neoplasms of the bile ducts received intraluminal local and systemic monotherapy with PDT, 19 patients in the comparison group did not receive PDT. The main group included 4 patients with stage III and 16 patients with stage IV according to the TNM classification. Of these, 20 patients had proximal cholangiocarcinoma: 4 patients – of type IIIa/IIIb and 16 patients – of type IV according to the Bismuth-Corlette classification. The comparison group included 3 patients with stage III and 16 patients with stage IV according to the TNM classification. Of these, 19 patients had proximal cholangiocarcinoma: 2 patients – of type II, 2 patients – of type IIIa/IIIb, 15 patients – of type IV according to the Bismuth-Corlette classification. A statistically significant increase in overall survival was found in patients who received PDT, with a median overall survival of 493±217 days (95% CI 276-710; $p < 0.05$) compared with 98±15 days (95% CI 83-100; $p < 0.05$) with PDT monotherapy [19]. In the main group, there were 2 cases of photosensitivity reaction, 5 cases of cholangitis (including 2 cholangitis complicated by sepsis), and 2 cases of stenosis after PDT. In the comparison group, there were 13 cases of cholangitis.

A meta-analysis with fixed effects of the proportions of individual studies and a pooled estimate of overall survival after PDT monotherapy was performed (Fig. 2).

The meta-analysis revealed a statistically significantly higher overall survival in the pooled assessment in the main groups where PDT was used – 339±161 days (95% CI 25-710; $p < 0.001$) compared to the comparison groups where PDT was not used – 83±16 days (95% CI 33-100; $p < 0.001$). The heterogeneity of the studies was considered statistically insignificant ($I2 = 29\%$, $p = 0.23$).

The probability of publication bias was assessed by visual analysis of the funnel plot (Fig. 3), where no visually significant asymmetry or disruption of the plot structure was detected, and the crossover point is in the area of no asymmetry ($p < 0.01$). The Begg and Mazumdar test also showed the absence of publication bias (Kendall's tau b -1.0000; $p = 0.3173$)

Then, a meta-analysis of the difference in the risks of adverse events in the compared groups was performed (Fig. 4), which revealed a statistically significantly lower risk (-0.2306; 95% CI -0.3917-0.0696; $p = 0.005$) of adverse events after PDT monotherapy compared to the comparison group. The heterogeneity of the studies was considered statistically insignificant ($I^2 = 0\%$, $p = 0.35$).

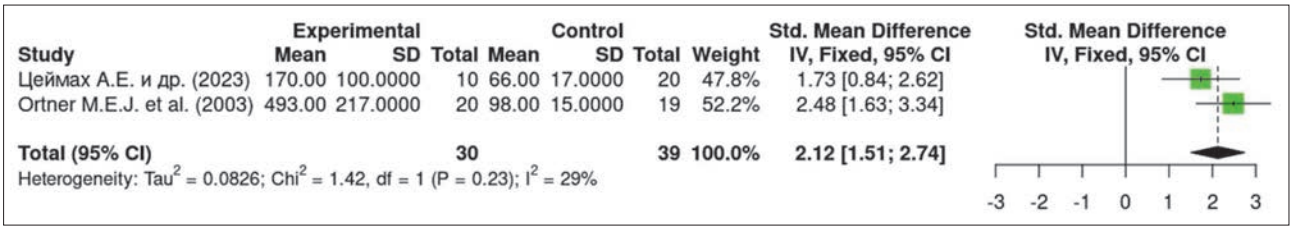

Рис. 2. Древовидная диаграмма с фиксированными эффектами, демонстрирующая анализ пропорций отдельных исследований и объединенную оценку общей выживаемости после монотерапии ФДТ.
Fig. 2. Forest plot of fixed effects demonstrating analysis of individual study proportions and pooled estimates of survival time following PDT monotherapy.

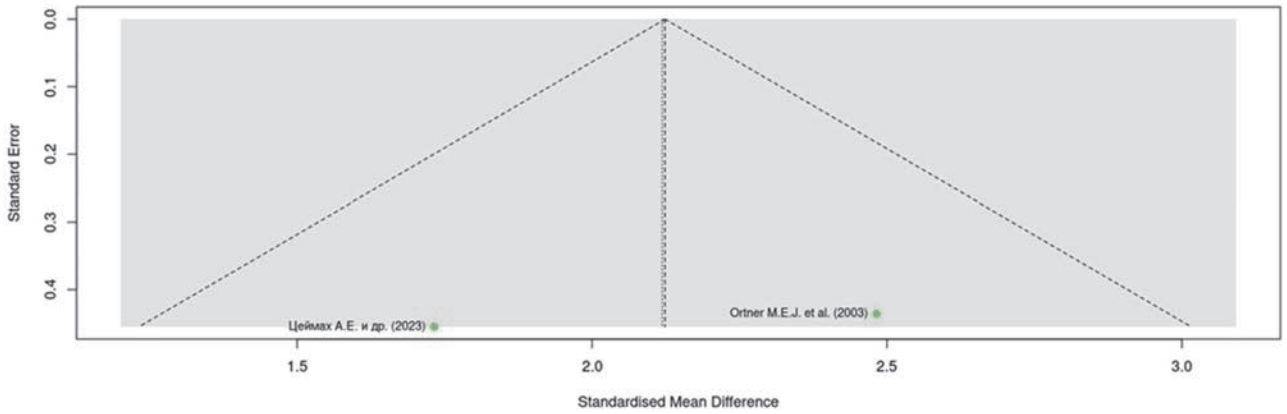

Рис. 3. Воронкообразный график для оценки вероятности наличия публикационной ошибки в объединенной оценке общей выживаемости после монотерапии ФДТ.
Fig. 3. Funnel plot to assess the likelihood of a publication error in pooled estimates of survival time following PDT monotherapy.

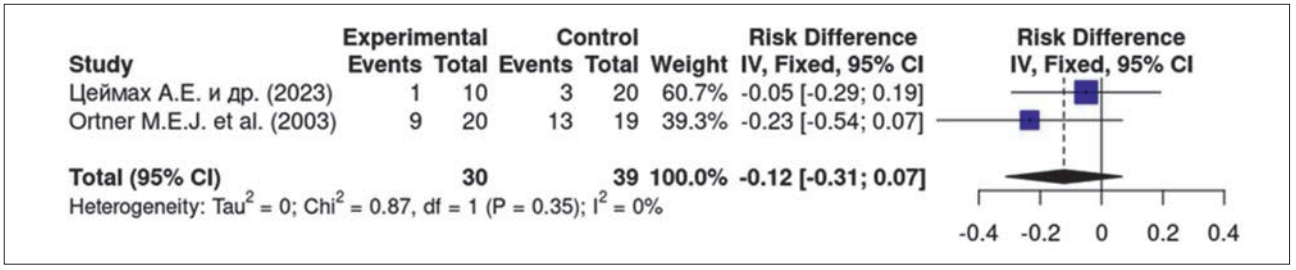

Рис. 4. Древовидная диаграмма с фиксированными эффектами, демонстрирующая анализ пропорций отдельных исследований и объединенного риска нежелательных явлений после монотерапии ФДТ.
Fig. 4. Forest plot of fixed effects demonstrating analysis of individual study proportions and pooled risk of adverse events after PDT monotherapy.

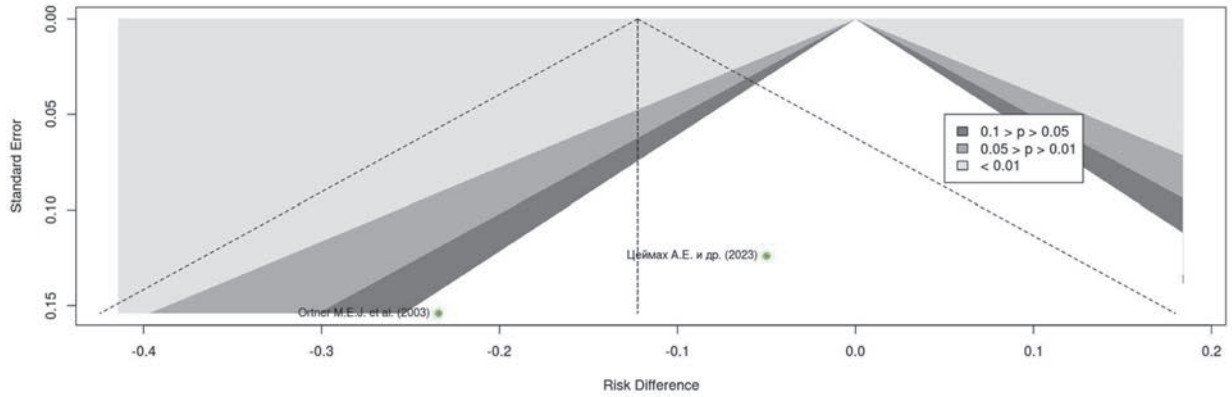

Рис. 5. Воронкообразный график для оценки вероятности наличия публикационной ошибки в объединенной оценке разницы рисков нежелательных явлений после монотерапии ФДТ.
Fig. 5. Funnel plot to assess the likelihood of a publication error in pooled estimates of risk difference of adverse events after PDT monotherapy.

The probability of the presence of a publication bias was assessed by visual analysis of the funnel plot (Fig. 5). No visually significant asymmetry or disruption of the graph structure was detected, and the crossover point is in the area of no asymmetry ($p < 0.01$). The Begg and Mazumdar test also showed the absence of a publication bias (Kendall's tau b – 1.0000; $p = 0.3173$).

Discusiion

Cholangiocarcinoma is a rare malignant neoplasm characterized by one of the worst prognoses among tumors of the digestive system [1, 3-5, 22-24]. About 80% of cholangiocarcinoma cases are diagnosed at a late stage, when radical surgical treatment is impossible [1, 3-5, 22-24, 25-26]. Chemotherapy and radiation therapy without surgery do not contribute to a significant increase in overall survival of patients [1, 3-5, 22-24]. Effective palliative treatment by decompression of the bile ducts to eliminate the clinical picture of mechanical jaundice and prevent cholangitis and sepsis are the main goal of surgical treatment and are the final intervention for most patients [1, 3-5, 22]. PDT is a promising treatment method for unresectable cholangiocarcinoma. Patients with unresectable cholangiocarcinoma have a median overall survival of 3 months without intervention and 4-10 months with bile duct decompression [1, 3-5, 22]. The presented systematic review and meta-analysis show that PDT can increase overall survival of patients with unresectable cholangiocarcinoma along with the absence of increased risks of adverse events compared with other methods of minimally invasive surgical treatment. A special role is played by targeted action on the tissue by performing choledochoscopy with intraluminal laser delivery to cholangiocarcinoma under visual control.

The aim of this meta-analysis was to evaluate the efficacy of palliative PDT for unresectable biliary tract malignancies. Survival meta-analysis revealed statistically significantly higher overall survival in the pooled assessment in the main groups where PDT was used – 332±229 days (95% CI 25-710; $p < 0.001$) compared to the comparison groups where PDT was not used – 82±23 days (95% CI 33-100; $p < 0.001$).

Meta-analysis of the difference in the risks of adverse events in the compared groups revealed a statistically significantly lower risk (-0.2306; 95% CI -0.3917-0.0696; $p = 0.005$) of adverse events after PDT monotherapy compared to the comparison group. The strength of the conducted meta-analysis is the high homogeneity and reliability of the obtained results, achieved by careful selec-

tion of studies with a homogeneous, clearly described design, study results and the same target access for local PDT – intraluminal under visual control.

Thus, the conducted meta-analysis allows to say with high statistical reliability that PDT is a promising and safe method of surgical intervention that can increase overall survival in patients with unresectable cholangiocarcinoma, and can be included in the complex treatment of this category of patients. The disadvantage of the conducted meta-analysis is the small number of patients in the study samples due to the rare occurrence of malignant neoplasms of the biliary system. Another weakness of the meta-analysis is the small number of studies included in the systematic review and meta-analysis. This is due to the fact that most published studies of the effectiveness of PDT evaluate PDT in combination with chemotherapy and/or radiation therapy.

At the same time, the synergy of PDT and chemotherapy, their possible antagonism associated with immunosuppression during chemotherapy treatment and the involvement of mechanisms of immune response stimulation in PDT have not been fully studied, and there is no consensus on PDT irradiation protocols in combination with radiation therapy. All these factors led to the inclusion of combined PDT as an exclusion criterion in the systematic review and meta-analysis. Another weakness of the meta-analysis is the differences in the PDT technique, which are characteristic of all studies in this area. This is due to both different photosensitizers and different parameters of cholangiocarcinoma irradiation.

Thus, given the above shortcomings, in order to obtain more reliable results and improve the quality of subsequent meta-analyses, large randomized studies of the effectiveness of PDT in unresectable cholangiocarcinoma are required. At the same time, the conducted meta-analysis proves the promise of PDT in the treatment of this category of patients.

Conclusion

The conducted meta-analysis demonstrated that PDT can be a method of choice in palliative complex treatment of patients with unresectable malignant neoplasms of the bile ducts, increasing the five-year survival of patients along with the absence of increased risks of postoperative complications in comparison with other methods of palliative surgical treatment.

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