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ORIGINAL ARTICLE

Intraoperative lymphography with indocyanine green experience in liver resection planning in patients with biliary cancer

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Abstract

Purpose of the study was to evaluate the feasibility of intraoperative lymphography with indocyanine green in cholangiocarcinoma and gallbladder cancer.

Patients and methods. The study included 26 patients with biliary cancer, who underwent intraoperative fluorescent lymphography with indocyanine green (ICG lymphography) during the period from April 2023 to January 2025 while planning lymph node (LN) dissection and liver resection. The lymph drainage from the liver and bile ducts was studied at 1, 3, 5, 10, 15, 30 ± 45 minutes from the ICG introduction with the determination of the first three stained LNs – sentinel lymph nodes (SLNs) – followed by subsequent LN dissection with the removal of regional LNs, as well as all stained LNs outside the areas of regional metastases. When technically possible, the planned volume of liver surgery and biliary tract resection was performed.

Results. In two cases (7.7 %) no SLN was detected, in this group there were no metastases in the LNs. In the remaining cases (92.3 %, *n* = 24), accumulation of ICG in one or more LNs was noted. LN invasion was noted in 12 patients. In this group, when using the first two stained LNs as SLNs, the sensitivity was 91.7 % (*n* = 11/12). Studying SLN 3 did not affect the sensitivity, but allowed identifying affected LNs outside the areas of regional metastases in two cases (7,7 %).

Conclusion. ICG lymphography is a promising method for determination of the SLNs and lymphatic drainage pathways in biliary cancer. It is advisable to evaluate the effect of LN dissection performed using fluorescence lymphography on long-term outcomes in patients with resectable biliary cancer.

Keywords:
bile duct cancer, gallbladder cancer, sentinel lymph nodes, fluorescent lymphography, lymph node dissection

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Compliance with ethical standards: the study was conducted in accordance with the ethical principles of the World Medical Association's Declaration of Helsinki (1964, revised 2013). The study protocol was approved by the Ethical Committee of the N.N. Blokhin National Medical Research Center of Oncology (Reference number: 12, October 26, 2023). Informed consent was obtained from all study participants.

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ОРИГИНАЛЬНАЯ СТАТЬЯ

Опыт применения интраоперационной лимфографии с индоцианином зеленым при планировании резекции печени у больных билиарным раком

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Аннотация

Цель исследования. Оценить целесообразность интраоперационной лимфографии с индоцианином зеленым (ИЦЗ) при холангиокарциноме и раке желчного пузыря в случае планирования резекции печени и лимфодиссекции.
Пациенты и методы. В исследование включены 26 больных билиарным раком, которым за период с 2023 по 2025 г. интраоперационно при планировании лимфодиссекции и резекции печени была применена флуоресцентная лимфография с индоцианином зеленым (ИЦЗ-лимфография). Изучался лимфоотток от печени и желчных протоков на 1-, 3-, 5-, 10-, 15-, 30-й минутах ± 45-й минутах от введения ИЦЗ с определением первых трех прокрашенных лимфатических узлов (ЛУ) – сторожевых лимфатических узлов (СЛУ) с последующей лимфодиссекцией регионарных ЛУ, а также всех прокрашенных ЛУ вне зон регионарного метастазирования. При технической возможности выполняли запланированный объем операции на печени и желчевыводящих путях.
Результаты. У двух пациентов (7,7 %) не было выявлено ни одного СЛУ: в этой группе метастазов в ЛУ не было. В остальных случаях (92,3 %, *n* = 24) отмечено накопление ИЦЗ в одном или нескольких ЛУ. Поражение ЛУ по данным морфологического исследования отмечено у 12 пациентов. В этой группе больных при использовании в качестве СЛУ первых двух прокрашенных ЛУ чувствительность метода составила 91,7 % (*n* = 11/12). Изучение третьего СЛУ не повлияло на чувствительность метода, но позволило выявить пораженные ЛУ вне зон регионарного метастазирования в двух случаях.
Заключение. ИЦЗ-лимфография – перспективный метод для определения СЛУ и путей лимфооттока при билиарном раке. Целесообразно оценить влияние лимфодиссекции выполненной с учетом флуоресцентной лимфографии на отдаленные результаты у больных с резектабельным билиарным раком.

Ключевые слова:
рак желчных протоков, рак желчного пузыря, сторожевые лимфатические узлы, флуоресцентная лимфография, лимфодиссекция

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Соблюдение этических стандартов: в работе соблюдались этические принципы, предъявляемые Хельсинкской декларацией Всемирной медицинской ассоциации (World Medical Association Declaration of Helsinki, 1964, ред. 2013). Исследование одобрено Этическим Комитетом при ФГБУ «НМИЦ онкологии им. Н.Н. Блохина» (выписка из протокола заседания №12 от 26.10.2023). Информированное согласие получено от всех участников исследования.

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INTRODUCTION

Biliary cancer, even in the group of operable patients, is characterized by a negative prognosis. The presence of lymphogenous metastases further worsens it [1, 2]. An increase in the number of lymphogenic metastases virtually eliminates the possibility of achieving long-term remission [1, 3].A high frequency of lymph node (LN) invasion in biliary cancer has been noted – about 30 % in intrahepatic cholangiocarcinoma (IHCC) [3, 4]. In the work of Ruzzenente A. et al. showed that even with a small size of the primary node of the IHCC – up to three centimeters inclusive – the frequency of detection of lymphogenous metastases reaches 30.3 %. A small tumor size, in the author's opinion, should not be a reason to avoid LN dissection [5]. With extrahepatic localization, the frequency of detection of lymphogenous metastases is also high [6]. Frequent invasion to LNs, along with other reasons, explains the need for routine regional LN dissection in patients with biliary tract cancer [7].

Some authors recommend performing a more extensive LN dissection in IHCC than is generally accepted [8]. Results of a study on the role of extended LN dissection in extrahepatic cholangiocarcinoma are awaited [9]. A review article by Li J. et al. notes the safety of extended LN dissection in perihilar tumor, as well as its possible advantages in more accurate staging and a positive effect on prognosis [10]. Several researchers prefer the method of a more extensive LN dissection in gallbladder cancer [11].

In surgical practice, the determination of sentinel lymph nodes (SLNs) using fluorescent lymphography with subsequent removal and morphological examination has recently found wide application. This method is most often used for breast cancer, melanoma, and in gynecological oncology [12, 13].

Moreover, given the variability of lymphatic drainage from the liver and biliary tract and, accordingly, a certain risk of LN damage outside the standard LN dissection zones in tumors of the hepatobiliary zone [14], it seems relevant to determine individual lymphatic outflow pathways from the affected structures in biliary cancer with the identification of SLN and LN dissection taking into account the results of lymphography [15].

Purpose of the study was to evaluate the feasibility of intraoperative lymphography with indocyanine green in cholangiocarcinoma and gallbladder cancer in case of planning liver resection and LN dissection.

PATIENTS AND METHODS

The study included 26 patients with biliary cancer who underwent regional LN dissection with preliminary ICG lymphography during surgery when planning liver resection for the period from 2023 to Jan 2025.

Prior to operation, a standard examination was performed including abdominal magnetic resonance imaging (MRI) with intravenous enhancement, computed tomography (CT) of the chest with intravenous enhancement, level of markers of CEA, CA 19–9 evaluation. If the presence of distant metastases was suspected, positron emission tomography combined with CT (PET/CT) was performed. The characteristics of the LNs of the zones of interest were noted, primarily the zones of regional metastasis. The interpretation of their condition by radiologists was noted.

To prepare a solution of the required concentration, 25 mg of ICG lyophilisate (Diagnostic Green GmbH, Germany or Mir-Pharm LLC, Russia) were dissolved in 20 ml of water for injection. During laparotomy, 1.0 ml of ICG solution was injected peritumorally under the liver capsule at each selected point along the periphery of the tumor(s) up to 5.0 ml in total. In case of gallbladder cancer or perihilar tumor, the drug was injected into the liver infiltration zone if there were signs of its involvement, as well as subserously into the wall of the gallbladder neck or cystic duct. Depending on the localization, size, and number of nodes, the injection was performed in different directions or from different positions. If it was necessary to create a wider infiltration zone around one node, the needle direction was changed without additional puncture of the capsule. The puncture points were sutured or coagulated to prevent ICG leakage. After administration of the solution, the accumulation of ICG in the lymphatic apparatus of the liver and bile ducts was observed using an infrared camera (VISERA ELITE II with a xenon light source CLV-S200-IR, OLYMPUS MEDICAL, Japan). Control points for evaluating the spread of ICG: 1, 3, 5, 10, 15, 30, 45 minutes. Whenever possible, additional observation of the spread of ICG was carried out in the intervals between control points.

If three SLNs were detected at 30 minutes or earlier, lymph drainage was not examined at 45 minutes. During this time, wide liver mobilization and LN dissection were not performed. Limited mobilization and adhesion dissection using power tools were allowed to minimize the flow of ICG from the dissected tissues.

After completion of ICG lymphography, LN dissection was performed with removal of regional LNs, as well as all LNs stained with ICG.

The three LNs that primary accumulated ICG were labeled as SLN 1, 2, and 3, respectively. The protocol noted the time of fluorescence appearance, macroscopic characteristics, localization, density, shape, size, and direct signs of metastatic lesions. Then, in the absence of contraindications, the planned volume of surgical treatment was performed.

Sensititvity was studied in the group of patients with metastatic LNs. This parameter was calculated as a percent of patients with invaded SLNs.

STUDY RESULTS

All patients underwent ICG lymphography with subsequent LN dissection of regional LNs, stained LNs, and extraregional removal of suspicious LNs. Only in one case, due to obvious signs of unresectability, limited lymphadenectomy with removal of three LNs was performed: all of them turned out to be affected. Curative liver resection was performed in 23 patients (88.5 %). The characteristics of all included patients are presented in Tables 1–3. Patients with IHCC predominated (57.7 %, *n* = 15). Four patients (15.4 %) were operated on for gallbladder cancer, two of them had previously undergone laparoscopic cholecystectomy for suspected cholecystitis. Another seven patients (26.9 %) underwent interventions for proximal extrahepatic cholangiocarcinoma. Radiologic methods in two patients after laparoscopic cholecystectomy did not reveal signs of recurrent tumor; the median maximum tumor size among the remaining patients (*n* = 24) was 45 mm.

The CA 19–9 level was elevated (more than 37 U/ml) in 10 patients (38.5 %), the median CA 19–9 was 22.56 U/ml. The CEA level was slightly elevated (more than 5 ng/ml) in three patients (11.5 %) – all up to and including 10 ng/ml. The AFP content in the blood serum was studied in the group of patients with IHCC, all had less than 5 U/ml.

Preoperative chemotherapy was administered to 18 patients (69.2 %). For the majority (88.9 %, *n* = 16/18), chemotherapy was administered according to the gemcitabine/cisplatin regimen; in two cases, durvalumab was added to this regimen. Two patients underwent therapy using other regimens. The median of the courses administered was 3.5 (3–8). Most patients with chemotherapy (72.2 %, *n* = 13/18) showed stabilization, four patients showed a partial response (22.2 %), and one patient showed progression (5.5 %). Photodynamic therapy was administered in one case, and stabilization was observed.

Table 1. Preoperative characteristics of the patients

Parameter		Value
Sex	Male, abs. (%)	10 (38.5 %)
	Female, abs. (%)	16 (61.5 %)
Age, median (minimum–maximum), years		65 (47–76)
Body mass index, median (minimum–maximum)		27.2 (19–37.6)
Diagnosis	Intrahepatic cholangiocarcinoma, abs. (%)	15 (57.7 %)
	Gallbladder cancer, abs. (%)	4 (15.4 %)
	Perihilar tumor, abs. (%)	7 (26.9 %)
Preoperative therapy	Chemotherapy	18 (69.2 %)
	Photodynamic therapy	1 (3.8 %)
	None	7 (26.9 %)
Visualization of the primary tumor according to examination data	Yes, abs. (%)	24 (92.3 %)
	No, abs. (%)	2 (7.7 %)
Primary tumor size according to examination data, median (minimum–maximum), mm		45 (10–105)
Signs of lymph node damage according to preoperative examination data	No, abs. (%)	7 (26.9 %)
	Lymphadenopathy, abs. (%)	12 (46.1 %)
	Suspicion, abs. (%)	2 (7.7 %)
	Affected, abs. (%)	5 (19.2 %)
CA 19-9 level before surgery, median (minimum–maximum), U/ml		22.56 (1.7–5256)
Preoperative CEA level, median (minimum–maximum), ng/ml		2.2 (0.5–10.0)

Based on the preoperative examination, suspicion or clear indication of lymphogenous metastases was obtained in 7 cases (26.9 %), and in another 12 (46.2 %) lymphadenopathy was noted, which required dynamic observation. In seven (26.9 %) patients, it was indicated that the LNs were unchanged.

According to the results of PET/CT, no signs of LN involvement were detected in five cases, in one case there was an indication of their involvement, and in another one there was a suspicion of lymphogenous metastases.

All patients (*n* = 26) underwent laparotomy, introduction of ICG with assessment of its lymphogenous spread with subsequent LN dissection. ICG was introduced from one puncture in 14 patients (53.8 %), from two – in nine patients (34.6 %), from three – in three patients (11.5 %). In two patients (7.7 %) no SLNs were detected, in the remaining cases accumulation of ICG in one or several LNs was noted (92.3 %, *n* = 24) with a median staining time of 15 min (1–30 min). Lymphogenous metastases (*n* = 12) were detected only in the group of patients in whom accumulation of the drug in at least one LN was noted (*n* = 24).

Figure 1 clearly shows how, in the first minute of observation after the introduction of ICG into the V and VIII segments of the liver, the fluorescent dye spreads along the lymphatic duct along the right edge of the common hepatic duct toward the 13th group LN, at the first stage bypassing the 12b group LN. In the third minute after the introduction of ICG, accumulation of the drug in the 13th group lymph node (SLN 1) was noted. During the morphological examination, it was the 13th group LN that was affected.

Exploratory operations were performed in three patients (11.5 %). In all cases local tumor spread was noted, in two patients peritoneal metastases were additionally detected. Resection of SIV–V liver segments was performed quite often (30.8 %, *n* = 8), in half of these patients – for gallbladder cancer (*n* = 4), in the rest – for IHCC (*n* = 4). Hemihepatectomy in combination with resection of bile ducts and removal of the first liver segment was performed in six patients (23.1 %).

The average duration of the operation was 300 min (90–420 min). The median time of curable resections, after excluding three exploratory operations, also reached

Table 2. Data revision and intraoperative parameters

Parameter		Value
Liver lobe	Right, abs. (%)	5 (19.2 %)
	Left, abs. (%)	5 (19.2 %)
	Both lobes, abs. (%)	7 (26.9 %)
	No signs of liver damage, abs. (%)	9 (34.6 %)
Lymph node involvement or suspicion of involvement based on revision data	Yes, abs. (%)	16 (61.5 %)
	No, abs. (%)	10 (38.5 %)
Operation	Extensive liver resection, abs. (%)	9 (34.6 %)
	Extensive resection with bile duct resection, abs. (%)	6 (23.1 %)
	SIV–V liver resection, abs. (%)	8 (30.8 %)
	Exploratory laparotomy, abs. (%)	3 (11.5 %)
Successful application of lymphography (presence of at least one SLN)	Yes, there are lymphogenous metastases, abs. (%)	12 (46.2%)
	Yes, but no lymphogenous metastases, abs. (%)	12 (46.2%)
	No SLN, abs. (%)	2 (7.7%)
White-test	Not conducted, abs. (%)	16 (61.5 %)*
	Conducted, positive, abs. (%)	2 (7.7 %)
	Conducted, negative, abs. (%)	8 (30.8 %)
Duration of surgery, median (minimum–maximum), min		300 (90–420)
Blood loss, median (minimum–maximum), ml		300 (50–1400)

* – in 6 cases there was resection of extrahepatic bile ducts, in 3 – no liver resection.

300 min (150–420 min). Blood loss in the overall group was 300 ml (50–1400 ml), after excluding exploratory operations – 350 ml (150–1400 ml).

No intraoperative complications (including those from the use of the method) were identified. Blood transfusion during surgery was performed in one case to a patient with a blood loss of 1400 ml.

Postoperative complications were noted in 10 patients (38.5 %). Bile leakage was detected in 8 patients (30.8 %). It should be noted that bile leakage was only in the group of patients without a white test. However, it was not possible to perform it in half of them due to resection of the bile duct due to perihilar tumor. Lymphorrea was noted in one patient (3.8 %), pancreatic fistula – also in one case (3.8 %). Postresection liver failure developed in two patients (7.8 %) – both patients were operated on due to perihilar tumor.

Complications of grade III and higher (Clavien – Dindo) developed in six patients (23.1 %). Complications of grade IIIA were noted in three cases (11.5 %), IVA – in two cases (7.7 %). Mortality was 3.8 % (*n* = 1), the cause of death was multiple organ failure against the background of intractable purulent-septic complications in the outcome of bile leakage. It should be noted that the white test was not performed intraoperatively in the deceased patient. Perhaps, if it had been performed, the defect in the bile duct wall would have been detected during the intervention, and the area of possible bile leakage would have been sutured. Despite the interventions performed, including bile duct stenting, sanitizing relaparotomy and a set of conservative measures, multiple organ failure progressed, which led to death.

The results of preoperative radiologic methods were assessed in the group of patients without LN

Table 3. Follow up period

Parameter	Value
Complications, abs. (%)	10 (38.5 %)
Bile leakage, abs. (%)	8 (30.8 %)
Post-resection liver failure, abs. (%)	2 (7.7 %)
Lymphorrea, abs. (%)	1 (3.8 %)
Complications ≥ grade III, abs. (%)	6 (23.1 %)
Mortality, abs. (%)	1 (3.8 %)
Number of affected LN in the group with metastases, median (minimum–maximum)	3 (1–9)
Number of LNs examined in the N + group, median (minimum–maximum)	10 (3–20)
Ratio of affected to examined nodes, median (minimum–maximum)	0.39 (0.005–1.0)
Number of LNs examined in the total group, median (minimum–maximum)	12 (3–25)

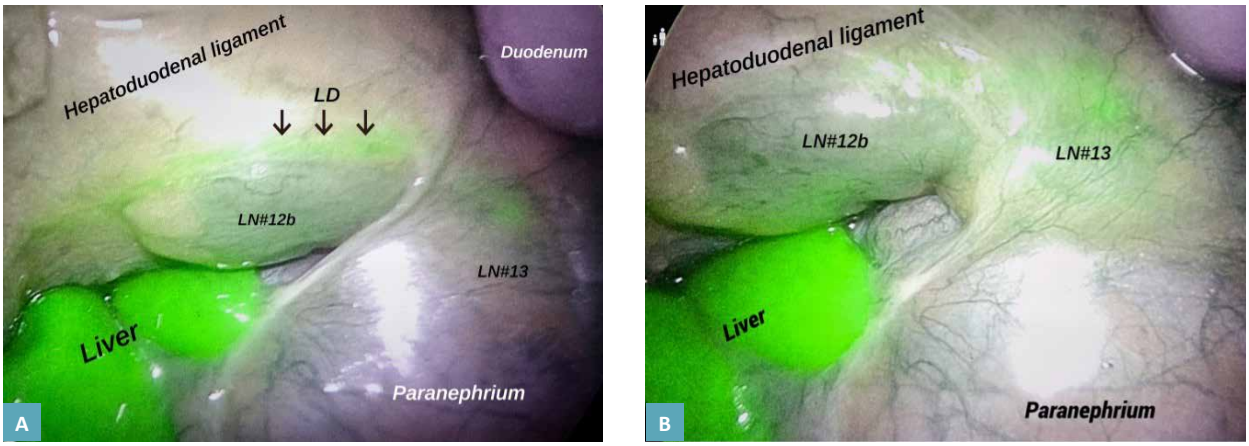

Fig. 1. Spread of ICG along the lymphatic duct (1A) and accumulation of the drug in the LNs of group 13 (1B)
LD – lymphatic duct, LN #12b – lymph nodes of group 12b, LN #13 – lymph nodes of group 13.

involvement (*n* = 14). Among patients without lymphogenous metastases at the preoperative stage, lymphadenopathy was indicated in seven cases (50.0 %), and LN involvement was suspected in one case (7.1 %). In six patients, LNs were not enlarged according to MRI/CT/PET data, and there were no indications of their possible involvement (42.9 %). There was no unambiguous interpretation in favor of metastatic LN involvement based on radiologic methods in any case.

It is also worth noting that in the group of patients without lymphogenous metastases, in half of the cases (50.0 %, *n* = 7), based on the data of intraoperative revision and palpation, the presence of LNs suspicious for metastatic lesions was noted. These LNs were round in shape and of dense consistency.

More detailed characteristics of patients with lymph node involvement (*n* = 12) are presented in the Table 4. In this group of patients, SLN 1 staining was noted in all patients, the median time of SLN 1 staining was 15 min (1–30 min). The median time of SLN 2 staining was 18 min (2–35 min). In one case in the group with positive LNs, there were no stained second-order LNs during the entire observation period. The median time of SLN 3 staining reached 30 min (5–45 min, in five cases, no "third-order" LN staining was detected).

Among patients with affected LNs (*n* = 12), in one case (patient No. 6) the result of the method application was false negative (8.3 %) – the only stained LN was not affected. It should be emphasized that it was in this patient that SLN 2 and, especially, SLN 3 were not detected. It should be noted that in less than half of patients with positive LNs, SLN 1 was affected (41.7 %, *n* = 5), while in nine patients (75.0 %), SLN 2 involvement was noted. In six cases, SLN 2 involvement was noted without SLN 1 involvement (50.0 %). So, when using the first two stained LNs as SLNs, the sensitivity of the method was 91.7 % – in 11 out of 12 cases with LN involvement, fluorescence of SLN 1 and/or SLN 2 was noted. Involvement of SLN 3 was detected in five patients, in all cases, involvement of SLN 3 was not isolated; in patients of this group, SLN 1 and/or SLN 2 were affected.

We note the non-standard invasion of LNs in four cases with the involvement of LNs No. 9, No. 7, No. 16 and No. 5, and in the first two cases their staining was noted at the third stage of accumulation of ICG.

Table 4 also shows that in two cases in the group of 12 patients with positive LNs, there was no indication of (or suspicion of) LN involvement either on preoperative examination or on revision (patient 6 and patient 8). In the absence of LN dissection, the operation would have been performed in a non-radical volume: the affected LNs would have been left.

Table 4. Characteristics of patients with lymphogenous metastases

No.	Tumor location or segment	SLN 1		SLN 2		SLN 3		Localization of affected LN	LN involvement by results			LNR
		N	mts	N	mts	N	Mts		MRI/CT	PET	revisions	
1	Gallbladder*	8	No	13	Yes	No	–	13**	susp	LA	No	2/17
2	2, 3, 4, 5, 8	12 b	Yes	12p	Yes	No	–	12 b, 12 p, 5	LA	–	susp	3/3
3	4, 5, 6, 7, 8	8	Yes	13	Yes	7	Yes	7, 8, 9**	LA	–	mts	4/18
4	Gallbladder	12 b	No	12c	Yes	No	–	12c	mts	–	mts	1/15
5	Perihilar tumor	12a	Yes	8	Yes	9	Yes	12 a, 12 c, 8**	LA	–	mts	9/12
6	4–5	12 b	No	No	–	No	–	13	LA	–	No	1/20
7	Perihilar tumor	12 a	No	8	Yes	13	No	8	mts	–	susp	1/17
8	Perihilar tumor	12 b	No	13	Yes	12 p	Yes	12 p, 8, 13, 5*	LA	–	No	6/9
9	2–3	13	No	12 b	Yes	No	–	12a, 12b, 8	mts	–	susp	4/8
10	2, 3, 4, 5	13	No	8	Yes	12 p	No	8, 5	No	–	susp	2/9
11	5, 6, 7, 8	13	Yes	8	No	12 p	Yes	12p, 13, 16	LA	mts	mts	3/10
12	Gallbladder	12a	Yes	8	No	12 p	Yes	12a, 12p, 13	mts	–	mts	3/8

mts – metastasis, LA – lymphadenopathy, susp – suspicion, LNR – lymph node ratio – the ratio between affected and removed lymph nodes.
* – after cholecystectomy, ** – more than one lymph node in the group is affected.

DISCUSSION

In addition to the main extension of surgery, standard interventions for perihilar tumor and IHCC, as well as for muscle-invasive gallbladder cancer, include LN dissection with removal of LNs of groups 12, 13, and 8 [16]. The need to perform routine LN dissection for biliary cancer is explained by a number of factors. The high level of detection of lymphogenous metastases in cholangiocarcinoma and gall bladder cancer being one of them [6]. The present study also showed that almost half of the patients operated on for biliary cancer had LN metastases detected during morphological examination – 12 out of 26 (46.2 %).

There are unresolved issues in determining LN involvement at the preoperative stage [17–19] and during revision [20].

We can also note that in the group of patients (n = 14) without LN involvement in the morphological examination, only one patient (7.1 %) had the results of radiological diagnostics at the preoperative stage indicating suspicion regarding the presence of metastases in LNs; in half of the cases, lymphadenopathy was noted (50.0 %, n = 7). However, in the same group of patients without detected lymphogenous metastases after routine LN dissection, in half of the cases (50.0 %, n = 7) during intraoperative revision, the presence of LNs suspicious for metastatic involvement based on visual and palpatory data was noted.

On the other hand, in two cases (16.7 %) in the group of patients with morphologically confirmed positive LNs, there was no indication of LN involvement or suspicion of LN involvement either based on preoperative examination or revision, which indicates the unreliability of these methods in determining lymphogenous metastases. If LN dissection had not been performed in these patients, the operation would have been non-radical.

It should be noted that at the preoperative stage, it is difficult for CT/MRI specialists to make an unambiguous conclusion about LN involvement. In the conclusion, half of the patients (n = 6/12) with subsequent LN metastases contain the wording "lymphadenopathy, dynamic observation required" – as in the group of patients without metastases (n = 7/14). Additional difficulties in interpreting the state of the LNs are caused by concomitant cholangitis, as well as the presence of stents/drains. It should be noted that in both cases of using PET/CT in the group of patients with LN metastases, its results contradicted the MRI data.

There may be certain preferences of surgeons in performing a more extensive LN dissection, for example, removal of LN of groups 1, 3, 5, 7 in case of left-sided localization of IHCC [2]. In IHCC, according to Zhu J, LN dissection plays a diagnostic role, helping more accurate determination of the stage and prognosis, without affecting the latter [3]. Let us note the controversial results of meta-analyses on this issue, including recently published ones [21, 22]. Only among patients with IHCC without regional metastases, the positive role of LN dissection was noted in a 2024 meta-analysis [21].

There are also supporters of a more extensive LN dissection, up to the removal of retroperitoneal LNs in gall bladder cancer, regardless of the status of the cystic LN [11]. The results of the ChiCTR1800015688 study on the feasibility of extended LN dissection in perihilar tumor are awaited [9]. However, Japanese researchers did not find any improvement in long-term results after extended CE with LN dissection of the liver porta compared to standard CE in stage T1b gall bladder cancer [23].

There is evidence that LN dissection may worsen immediate results. Knitter S. et al. showed that even when performing standard LN dissection in a combined group of patients, which included patients with colorectal cancer metastases to the liver, as well as patients with IHCC and hepatocellular carcinoma, when performing LN dissection, more time was required for the operation ($p < 0.001$), biliary fistulas ($p < 0.003$), PRLI ($p < 0.001$), bleeding ($p = 0.027$) developed more often in the postoperative period. However, in a subgroup analysis among patients with IHCC, no significant increase in complications was noted, the authors only indicate an increase in the duration of the operation and a longer postoperative period of hospital stay ($p < 0.001$ and $p = 0.046$, respectively) [24].

In our work, all patients underwent regional LN dissection, as well as removal of stained LNs and suspicious LNs outside the areas of regional metastasis. The median of removed LNs in the overall group was 12 (3–25). The median of removed LNs in the group of patients with LN metastases reached 10 (3–20). Only in one case, LN dissection was stopped due to the detection of obvious signs of unresectability; 3 LNs were removed. The ratio of affected to examined nodes in the group with LN metastases was 0.39 (0.005–1.0). In our work, there was no direct comparison of complications in the group of patients with ICG lymphography with subsequent LN dissection and without it. Nevertheless, we note that in the case of using ICG lymphography, there were no intraoperative complications, including those associated with the use of ICG.

It should be noted that lymph drainage from the intrahepatic and extrahepatic bile ducts and liver is variable [14, 15], which explains the risk of metastatic lesions of the lymphatic apparatus outside the areas of regional metastasis in bile duct and gallbladder cancer. A wider LN dissection, in which not only the tissue with LNs outside the hepatoduodenal ligament, retropancreatoduodenal zone and along the common hepatic artery are removed, is aimed at achieving greater radicalism [2, 3, 9, 10, 11].

It should be noted that detection of affected LNs may influence treatment tactics. There is evidence on the advisability of adjuvant chemoradiotherapy in patients with resectable extrahepatic biliary cancer with regional metastases. This approach allowed achieving a similar two-year overall survival in the group with positive LNs compared to the group in which there was no LN involvement. In other words, radiation therapy leveled the negative impact of lymphogenous metastases on the prognosis. In addition, the advantage of the combined approach was noted in the group of patients with LN metastases when compared with the historical control, in which radiation therapy was not performed. Two-year disease-free survival level reached 49.8 % in the main group versus 29.7 %, $p = 0.004$ [25].

The extend of additional LN dissection often depends on the preferences of the clinic and the experience of the surgeon [4, 11, 26]. The use of lymphography in determining the main route of lymphatic drainage from the liver is of interest [15]. The use of ICG lymphography in real clinical practice with determination of the predominant route of lymphatic drainage and marking of the SLN with subsequent LN dissection is promising [8].

The results of the present study showed that almost all patients ($n = 24/26$) who underwent ICG lymphography had at least one SLN detected. It should be noted that in the group where SLNs were not detected, standard LN dissection was performed: no lymphogenous metastases were detected.

Among patients with lymphogenous metastases ($n = 12$), in one case the result of the method application was false negative (8.3 %) – the only stained LN was not affected, while damage was noted in the LNs of another group that did not accumulate ICG during 45 min of observation using an infrared camera.

On the other hand, the remaining 11 patients with lymphogenous metastases had lesions in SLN 1 and/or SLN 2, i.e. the sensitivity of the method was 91.7 % when using the first two stained LNs as SLNs. It should be noted that only five patients (41.7 %) had lesions in SLN 1, and in three of them – in combination with lesions in SLN 2. In half of the cases, metastases were detected in SLN 2 without lesions in SLN 1 (50.0 %, $n = 6$).

The use of stained third-order LNs did not increase the sensitivity of the method, but allowed us to identify non-standard LN lesions in two cases involving LNs No. 9 and No. 7.

CONCLUSION

In cases of IHCC, perihilar tumor and gallbladder cancer, LN dissection with removal of LNs of groups 12, 13 and 8 remains a standard method in addition to the main extend of intervention. The absence of signs of LN involvement according to revision and examination data does not exclude their presence. It is necessary to take into account the variability of lymphatic drainage from the liver and biliary tract in case of their tumor damage, for example, in IHCC with invasion to the left lobe of the liver. For this purpose, ICG lymphography can be used as a promising method for determining the SLN and lymphatic drainage pathways in biliary cancer. It is advisable to evaluate the effect of LN dissection performed taking into account ICG lymphography on the long-term results in operable patients with biliary tract cancer.

References

1. van Keulen AM, Olthof PB, Cescon M, Guglielmi A, Jarnagin WR, Nadalin S, et al. Actual 10-Year Survival after Resection of Perihilar Cholangiocarcinoma: What Factors Preclude a Chance for Cure? Cancers (Basel). 2021 Dec 13;13(24):6260. https://doi.org/10.3390/cancers13246260
2. Zhang XF, Xue F, Dong DH, Weiss M, Popescu I, Marques HP, et al. Number and Station of Lymph Node Metastasis After Curative-intent Resection of Intrahepatic Cholangiocarcinoma Impact Prognosis. Ann Surg. 2021 Dec 1;274(6):e1187–e1195. https://doi.org/10.1097/sla.0000000000003788
3. Zhu J, Liu C, Li H, Ren H, Cai Y, Lan T, Wu H. Adequate lymph node dissection is essential for accurate nodal staging in intrahepatic cholangiocarcinoma: A population-based study. Cancer Med. 2023 Apr;12(7):8184–8198. https://doi.org/10.1002/cam4.5620
4. Zhang XF, Xue F, Weiss M, Popescu I, Marques HP, Aldrighetti L, et al. Lymph Node Examination and Patterns of Nodal Metastasis Among Patients with Left- Versus Right-Sided Intrahepatic Cholangiocarcinoma After Major Curative-Intent Resection. Ann Surg Oncol. 2023 Mar;30(3):1424–1433. https://doi.org/10.1245/s10434-022-12797-2
5. Ruzzenente A, Conci S, Viganò L, Ercolani G, Manfreda S, Bagante F, et al. Role of Lymph Node Dissection in Small (≤3 cm) Intrahepatic Cholangiocarcinoma. J Gastrointest Surg. 2019 Jun;23(6):1122–1129. https://doi.org/10.1007/s11605-019-04108-0
6. Marinelli I, Guido A, Fuccio L, Farioli A, Panni V, Giaccherini L, et al. Clinical Target Volume in Biliary Carcinoma: A Systematic Review of Pathological Studies. Anticancer Res. 2017 Mar;37(3):955–961. https://doi.org/10.21873/anticanres.11404
7. Vogel A, Bridgewater J, Edeline J, Kelley RK, Klümpen HJ, Malka D, et al.; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. Biliary tract cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2023 Feb;34(2):127–140. https://doi.org/10.1016/j.annonc.2022.10.506

8. Zhang Y, Zhang Y, Zhu J, Tao H, Liang H, Chen Y, et al. Clinical application of indocyanine green fluorescence imaging in laparoscopic lymph node dissection for intrahepatic cholangiocarcinoma: A pilot study (with video). Surgery. 2022 Jun;171(6):1589–1595. https://doi.org/10.1016/j.surg.2021.09.032
9. He M, Xu X, Feng H, Chen W, Liu H, Zhang Y, et al. Regional lymphadenectomy vs. extended lymphadenectomy for hilar cholangiocarcinoma (Relay-HC trial): study protocol for a prospective, multicenter, randomized controlled trial. Trials. 2019 Aug 23;20(1):528. https://doi.org/10.1186/s13063-019-3605-z
10. Li J, Zhou MH, Ma WJ, Li FY, Deng YL. Extended lymphadenectomy in hilar cholangiocarcinoma: What it will bring? World J Gastroenterol. 2020 Jun 28;26(24):3318–3325. https://doi.org/10.3748/wjg.v26.i24.3318
11. Vega EA, Vinuela E, Yamashita S, Sanhueza M, Cavada G, Diaz C, et al. Extended Lymphadenectomy Is Required for Incidental Gallbladder Cancer Independent of Cystic Duct Lymph Node Status. J Gastrointest Surg. 2018 Jan;22(1):43–51. https://doi.org/10.1007/s11605-017-3507-x
12. van Dam MA, Bijlstra OD, Faber RA, Warmerdam MI, Achiam MP, Boni L, et al. Consensus conference statement on fluorescence-guided surgery (FGS) ESSO course on fluorescence-guided surgery. Eur J Surg Oncol. 2024 Feb;50(2):107317. https://doi.org/10.1016/j.ejso.2023.107317
13. Tikhonovskaya MN, Shevchuk AS. Sentinel lymph node detection in early stage ovarian cancer: the primary experience in N.N. Blokhin National medical Research Center of Oncology. Pelvic Surgery and Oncology. 2022;12(3):19–25. (In Russ.). https://doi.org/10.17650/2686-9594-2022-12-3-19-25
14. Yong TL, Houli N, Christophi C. Anatomy of hepatic lymphatics and its implications in hepatic malignancies. ANZ J Surg. 2016 Nov;86(11):868–873. https://doi.org/10.1111/ans.13662
15. Frenkel NC, Poghosyan S, Verheem A, Padera TP, Rinkes IHMB, Kranenburg O, Hagendoorn J. Liver lymphatic drainage patterns follow segmental anatomy in a murine model. Sci Rep. 2020 Dec 11;10(1):21808. https://doi.org/10.1038/s41598-020-78727-y
16. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, et al. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin. 2017 Mar;67(2):93–99. https://doi.org/10.3322/caac.21388
17. Kolck J, Auer TA, Walter-Rittel T, Hosse C, Elkilany A, Marth AA, et al. Prediction of regional lymph node metastasis in intrahepatic cholangiocarcinoma: it's not all about size. Abdom Radiol (NY). 2023 Oct;48(10):3063–3071. https://doi.org/10.1007/s00261-023-03991-1
18. Kim YY, Yeom SK, Shin H, Choi SH, Rhee H, Park JH, et al. Clinical Staging of Mass-Forming Intrahepatic Cholangiocarcinoma: Computed Tomography Versus Magnetic Resonance Imaging. Hepatol Commun. 2021 Dec;5(12):2009–2018. https://doi.org/10.1002/hep4.1774
19. Lamarca A, Barriuso J, Chander A, McNamara MG, Hubner RA, ÓReilly D, et al. 18F-fluorodeoxyglucose positron emission tomography (18FDG-PET) for patients with biliary tract cancer: Systematic review and meta-analysis. J Hepatol. 2019 Jul;71(1):115–129. https://doi.org/10.1016/j.jhep.2019.01.038
20. Gyoten K, Kuriyama N, Maeda K, Ito T, Hayasaki A, Fujii T, et al. Safety and efficacy of neoadjuvant chemotherapy based on our resectability criteria for locally advanced perihilar cholangiocarcinoma. Langenbecks Arch Surg. 2023 Jul 1;408(1):261. https://doi.org/10.1007/s00423-023-03000-5
21. Yeow M, Fong KY, Zhao JJ, Tan AYH, Koh YX, Kam JH, et al. Value of lymph node dissection in intrahepatic cholangiocarcinoma: a systematic review and meta-analysis. HPB (Oxford). 2024 Feb;26(2):161–170. https://doi.org/10.1016/j.hpb.2023.11.007
22. Atif M, Borakati A, Mavroeidis VK. Role of routine lymph node dissection alongside resection of intrahepatic cholangiocarcinoma: Systematic review and meta-analysis. World J Gastrointest Oncol. 2023 Nov 15;15(11):2017–2032. https://doi.org/10.4251/wjgo.v15.i11.2017
23. Yuza K, Sakata J, Prasoon P, Hirose Y, Ohashi T, Toge K, et al. Long-term outcomes of surgical resection for T1b gallbladder cancer: an institutional evaluation. BMC Cancer. 2020 Jan 6;20(1):20. https://doi.org/10.1186/s12885-019-6507-2
24. Knitter S, Raschzok N, Hillebrandt KH, Benzing C, Moosburner S, Nevermann N, et al.; members of StuDoQ|Liver of Deutsche Gesellschaft für Allgemein-und Viszeralchirurgie/StuDoQ. Short-term postoperative outcomes of lymphadenectomy for cholangiocarcinoma, hepatocellular carcinoma and colorectal liver metastases in the modern era of liver surgery: Insights from the StuDoQ|Liver registry. Eur J Surg Oncol. 2024 Apr;50(4):108010. https://doi.org/10.1016/j.ejso.2024.108010
25. Gholami S, Colby S, Horowitz DP, Guthrie KA, Ben-Josef E, El-Khoueiry AB, et al. Adjuvant Chemoradiation in Patients with Lymph Node-Positive Biliary Tract Cancers: Secondary Analysis of a Single-Arm Clinical Trial (SWOG 0809). Ann Surg Oncol. 2023 Mar;30(3):1354–1363. https://doi.org/10.1245/s10434-022-12863-9
26. Sposito C, Maspero M, Cucchetti A, Mazzaferro V. A snapshot on current approaches to lymphadenectomy in liver resection for intrahepatic cholangiocarcinoma: results from an international survey. Updates Surg. 2024 Sep;76(5):1797–1805. https://doi.org/10.1007/s13304-024-01852-0

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