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DETECTION OF LIVER MALIGNANT TUMORS AND INTRAHEPATIC BALL DUCTS IN THE REPUBLIC OF SAKHA (YAKUTIA)

The article presents a cross-sectional retrospective study of cases of malignant neoplasms of liver and intrahepatic bile ducts (C22) in the Republic of Sakha (Yakutia) (RS (Y)) in 2010–2019 based on statistical registration forms No. 7 and 35. During the study period, significantly increased incidence and mortality rates from malignant neoplasms of the liver and intrahepatic bile ducts were recorded. At the same time, the proportion of detection of the studied pathology at early stages remains low, despite the strengthening of diagnostic measures within the framework of preventive examinations and screening programs. In the dynamics for 2010–2019, an increase in the prevalence of malignant neoplasms of the liver and intrahepatic bile ducts is noted in the RS (Y), but the number of patients under observation for 5 years or more tends to decrease. The obtained data substantiate the need to improve organizational approaches to early diagnosis and treatment, optimize patient routing, and study precancerous factors of liver cancer of population of the Republic of Sakha (Yakutia).

Keywords: malignant neoplasms of liver and intrahepatic bile ducts, cancer, detectability, the Republic of Sakha (Yakutia).

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Introduction. There are enough works in the literature devoted to the study of pre-cancerous genesis of malignant neoplasms of the liver and bile ducts. It is described that the causes of liver cancer have ethnic, territorial, and social heterogeneity. It is well known that viral hepatitis C, alcoholic liver disease, and fatty hepatosis are among the top three factors in the development of liver cancer in developed countries. In developing countries where hepatitis B vaccination is not established, the main cause of liver cancer is hepatitis B. Due to the increasing global incidence of liver cancer and the national, regional, and population specificity of the causes of this cancer, targeted prevention strategies for its various etiologic types are currently needed to reduce the burden of liver cancer [1].

The highest incidence of liver cancer is observed in such regions of the world as East and Southeast Asia, North and West Africa [2]. These differences are due to the prevalence of risk factors, which include chronic hepatitis B and C [3,4], hemochromatosis [5], diabetes mellitus [6], cirrhosis and fatty liver disease [7], obesity [8], alcohol abuse [9], exposure to certain carcinogens, hormones, dyes [10, 11], aflatoxins [12], etc. Of these, more than half of the cases of hepatocellular carcinoma (HCC) are associated with viral hepatitis B (HBV). In regions with a high prevalence of this infection, the proportion of HCC cases reaches 70–80% [3]. According to case-control studies, the relative risk of HCC among HBV-infected people varies from 5 to 49, according to cohort studies - from 7 to 98 [3]. According to the results of multicenter epidemiological studies, it was proven that viral hepatitis B and C were the main cause of liver cancer and death of patients. It is described that viral hepatitis B is most common in the countries of Southeast Asia. Statistics have shown that 85% of the world's cases of liver cancer and deaths from this disease for the period from 1990-2017 occur in these countries. Approximately 15% of the total number of deaths and cases of liver cancer in the world are caused by alcoholism. Alcohol can cause liver cirrhosis and create an environment favorable for viral hepatitis infection. In fact, the risk of developing liver cancer doubles in individuals who have chronically consumed > 80 g of alcohol for > 10 years. According to data from 1990 to 2017, alcoholism was the leading cause of liver cancer in several European countries (Bulgaria, Croatia, Czech Republic, Hungary, Poland, Slovakia, Austria, Denmark, Germany, Luxembourg, Sweden, Canada and Greenland). Hepatitis C and alcohol abuse were the leading risk factors for liver cancer in developed countries (UK, USA, Italy and Canada). More than 30% of the total number of liver cancer-related deaths and cases in Central Europe, Eastern Europe, Australia and Western Europe were caused by alcohol consumption [1].

The Sakha Republic (Yakutia), which is part of the Arctic region, is the subject of the Russian Federation (RF) with the highest incidence rates of malignant neoplasms of the liver and intrahepatic bile ducts in the country. The population of the Republic of Sakha (Yakutia) as of January 2020 reached 972 000 people with a population density of 0.32 people/km^2.

The COVID-19 pandemic has caused significant disruptions in the provision of cancer care worldwide, including delays in the organization of screening, follow-up of patients at high risk for developing HCC, referral to specialists, diagnosis, therapy, and follow-up. Although cancer screening resumed in many countries in the summer of 2020, the long-term impact of missed screenings is not

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well understood. According to studies, skipping recommended cancer screenings and fewer doctor visits during the pandemic lead to an increase in the number of primary diagnoses at late stages, a decrease in the number of malignant neoplasms detected during dispensary observation or incidental detection, as well as a longer-term increase in cancer mortality [13; 14; 15; 16].

To conduct the epidemiological analysis, data from the pre-pandemic period (2010–2019) were used, which made it possible to establish reference values for the subsequent study of the impact of the COVID-19 pandemic on the dynamics of morbidity and the structure of the stages of detected cases. The data obtained are key to the correct interpretation of changes associated with the peculiarities of the organization of the healthcare system during the pandemic (2020–2021) and their long-term consequences, including possible long-term shifts in the epidemiological indicators of liver cancer. The aim of this study is to analyze the detection rates of malignant neoplasms of the liver and intrahepatic bile ducts (C22) in the Republic of Sakha (Yakutia) for the period from 2010 to 2019.

Materials and methods. Open data from the P.A. Herzen Moscow Oncology Research Institute - a branch of the National Medical Research Center of Radiology of the Ministry of Health of the Russian Federation on the localization of "liver and intrahepatic bile ducts" (C22 ICD-10) since 2011 (up to and including 2010, data on liver cancer were not collected separately), data from the State Budgetary Institution of the Republic of Sakha (Yakutia) "Yakutsk Republican Oncology Dispensary" (statistical forms No. 7, 35) have been used in the work. Information on patients registered in oncological institutions of the Russian Federation for 5 years or more from the moment of diagnosis of malignant neoplasm of the liver and intrahepatic bile ducts, from the number registered at the end of the reporting year, has been entered into statistical form No. 35 of the federal statistical observation since 2011 (since 2016, form No. 7). Therefore, when calculating the share of the contingent of patients registered in oncological institutions for 5 years or more, data for 2011-2014 were used.

Results. In 2015-2019, the frequency of cases of active detection of malignant neoplasms of the liver and intrahepatic bile ducts during preventive and screening examinations of the population increased from 2.7% in 2011-2014 to 16.8%. (Table). However, the proportion of cases with morphological verification of the diagnosis continues to remain low, and amounts to 49 and 42%, respectively, during these time periods.

Indicators of liver cancer diagnostic activity and five-year survival, in %

Indicator	2011–2014*		2015–2019	
	РС (Я)	РФ	РС (Я)	РФ
Actively detected, %	2,7	3,8	16,8	6,4
Diagnosis confirmed morphologically, %	49,3	50,8	42,3	66,1
detected: stage1	1,2	1,3	1,8	2,7
Stage 2	3,9	6,8	11,4	10,2
Stage3	33,7	22,2	45,1	22,8
Stage3	61,3	57,0	41,1	57,4
Stage not established	0,0	12,8	0,5	5,8
Percentage of those registered for 5 years and more	31,1	26,9	22,2	31,3

Note: *The figures are calculated for 2011–2014, since in 2010, data on liver cancer in Russia were not collected separately.

In the last years of the study period, the detection rate of liver cancer and intrahepatic bile duct cancer at early stages improved and reached the average Russian values, as a result of which the share of advanced cases decreased from 61.3% to 41.1%. If we take into account the indicators of the Russian Federation as a whole, then for the analyzed periods the share of cases with morphological verification of the diagnosis is on average higher than for the RS (Ya). This is due to the instrumental and laboratory methods of diagnosis, and with the introduction of a hepatospecific method of radiation diagnostics. In 2015-2019, the proportion of liver cancer and intrahepatic bile duct cancer cases detected at stages 1 and 2 of the disease in the Republic of Sakha (Yakutia) and the Russian Federation as a whole are generally comparable (13.2 and 12.9%, respectively), and the proportion of advanced cases (at stage 4) is lower in the Republic of Sakha (Yakutia). In 2015-2019, the proportion of patients under the supervision of an oncology institution for 5 years or more in the Republic of Sakha (Yakutia) amounted to 22%, and in the Russian Federation as a whole - 31% of the number of those registered at the end of the year. At the same time, in 2015-2019, compared with the period 2010-2014, the proportion of those registered for 5 years or more in the Republic of Sakha (Yakutia) decreased by 1.4 times, in the Russian Federation as a whole it increased by 16.4%.

In 2011 and 2019, the number of patients with malignant neoplasms of the liver and intrahepatic bile ducts under observation in the oncology dispensary of the Republic of Sakha (Yakutia) for 5 years or more did not change (41 and 40 people, respectively), but during this period until 2014, there was an increase of 1.2 times (49 people) with a subsequent decrease. From 2011 to 2019, there was an increase in the number of all patients registered with a diagnosis of malignant neoplasms of the liver and intrahepatic bile ducts by 1.6 times (2011 - 138, 2019 - 218 people). In the Russian Federation as a whole, there is an increase in both the number of patients diagnosed with cancer of the liver and intrahepatic bile ducts who are under observation in oncological institutions for 5 years or more, and the number of all patients registered with a diagnosis of cancer of the liver and intrahepatic bile ducts, by 1.7 and 1.4 times, respectively (1817 and 6670 people in 2011, 3076 and 9057 in 2019, respectively).

Discussion. The Republic of Sakha (Yakutia) is a subject of the Russian Federation with the highest rates of morbidity and mortality from cancer of the liver and intrahepatic bile ducts. Over the study period from 2015-2019, the activity of detecting cancer of the liver and intrahepatic bile ducts has significantly increased as part of preventive and screening examinations of the population. Morphological verification of the diagnosis lags behind the Russian average, but it is necessary to take into account that, according to the clinical recommendations of the Ministry of Health of the Russian Federation, it is possible to establish a diagnosis of hepatocellular carcinoma based on the results of clinical and radiological data, which accounts for about 80% of the structure of malignant neoplasms of the liver and intrahepatic bile ducts.

Although the level of detection of malignant neoplasms of the liver and intrahepatic bile ducts at early stages has increased with a decrease in the share of diagnosis of this pathology at late stages, the detection rates at stages 1-2 continue

to be low, compared with the indicators of the Russian Federation as a whole, but have a tendency to increase. In 2015-2019, the detection rates of liver cancer and intrahepatic bile ducts at stages 1 and 2 of the disease in the Republic of Sakha (Yakutia) and the Russian Federation as a whole are comparable, while the diagnosis of cancer at stage 4 is lower in the Republic of Sakha (Yakutia) than the Russian average.

In the Republic of Sakha (Yakutia) in 2015-2019, the proportion of patients with this malignant neoplasm who are under observation for 5 years or more is approximately 10% lower compared to the data for the Russian Federation as a whole. There is some significant decrease in the proportion of this category of patients in 2015–2019 compared to 2010–2014. In the Republic of Sakha (Yakutia) for 2011–2019, an increase in the total number of patients registered for dispensary care with a diagnosis of malignant neoplasms of the liver and intrahepatic bile ducts was revealed compared to the all-Russian data.

Conclusion. Thus, the conducted analysis of the epidemiological indicators of malignant neoplasms (MN) of the liver and intrahepatic bile ducts in the Republic of Sakha (Yakutia) for 2010–2019 shows a high incidence rate, improved early detection rates, and a slight tendency to increase of the survival rate of 5 years or more when analyzed by year.

Moreover, our analysis of pre-pandemic data (2010–2019) allowed us to establish important reference values for epidemiological indicators of malignant liver neoplasms. These data are of particular importance in the context of assessing the impact of the COVID-19 pandemic on oncology services, particularly in liver cancer. The results obtained create a scientific basis for an objective analysis of the changes that occurred in the healthcare system in 2020–2021 and their potential long-term consequences, and lay the methodological foundation for a subsequent comprehensive analysis of the impact of the pandemic crisis on oncology care for the population.

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References

1. Zikiryakhodjaev A.D., Saribekyan E.K., Bagdasarova D.V., et al. Biopsiya storozhevogo limfaticheskogo uzla pri rake molochnoj zhelezy s primeneniem metoda fluorescentnoj vizualizacii krasitelya indocianin zelenyj [Sentinel lymph node biopsy in breast cancer using the indocyanine green fluorescent imaging method]. Biomedical Photonics [Biomedical Photonics. 2019; 8 (4): 4–10 (In Russ).]. doi: 10.24931/2413–9432–2019–8–4–4–10.

2. Krivorotko P, Zernov K, Paltuev R, et al. Biopsiya signal'nyh limfaticheskih uzlov pri rannem rake molochnoj zhelezy: opyt NII onkologii im. N.N. Petrova [Biopsy of signaling lymph nodes in early breast cancer: the experience of the N.N. Petrov Research Institute of Oncology]. Voprosy onkologii [Issues of oncology. 2017; 63(2): 267-273 (In Russ.).] https://doi.org/10.37469/0507-3758 .

3. Sostoyanie onkologicheskoj pomoshchi naseleniyu Rossii v 2022 godu [The state of oncological care for the Russian population in 2022. Edited by A.D. Kaprin, V.V. Starinsky, A.O. Shakhzadova. Moscow: P.A. Herzen Moscow Institute of Medical Sciences − branch of the Federal State Budgetary Institution "NROI of Radiology" of the Ministry of Health of the Russian Federation, 2023; 254 p. (In Russ.).]

4. Akrida I, Michalopoulos NV, Lagadinou M, Papadoliopoulou M, Maroulis I, Mulita F. An Updated Review on the Emerging Role of Indocyanine Green (ICG) as a Sentinel Lymph Node Tracer in Breast Cancer. Cancers (Basel). 2023 Dec 8;15(24):5755. doi: 10.3390/cancers15245755. PMID: 38136301; PMCID: PMC10742210.

5. Alsunitan RI, Al-Saif A, Alyousef BA, Alghamdi SM, Bugshan SA. Axillary Recurrence in Breast Cancer Patients After Negative Sentinel Lymph Node Biopsy: Retrospective Cohort Study From Riyadh, Saudi Arabia. Cureus. 2021 Dec 3;13(12):e20132. doi: 10.7759/cureus.20132. PMID: 34900499; PMCID: PMC8649977.

6. Goonawardena J, Yong C, Law M. Use of indocyanine green fluorescence compared to radioisotope for sentinel lymph node biopsy in early-stage breast cancer: systematic review and meta-analysis. Am J Surg. 2020 Sep;220(3):665-676. doi: 10.1016/j.amjsurg.2020.02.001. Epub 2020 Feb 7. PMID: 32115177.

7. Inoue T, Nishi T, Nakano Y, Nishimae A, Sawai Y, Yamasaki M, Inaji H. Axillary lymph node recurrence after sentinel lymph node biopsy performed using a combination of indocyanine green fluorescence and the blue dye method in early breast cancer. Breast Cancer. 2016 Mar;23(2):295-300. doi: 10.1007/s12282-014-0573-8. Epub 2014 Oct 28. PMID: 25348937.

8. Jung SY, Han JH, Park SJ, Lee EG, Kwak J, Kim SH, Lee MH, Lee ES, Kang HS, Lee KS, Park IH, Sim SH, Jeong HJ, Kwon Y, Lee DE, Kim SK, Lee S. The Sentinel Lymph Node Biopsy Using Indocyanine Green Fluorescence Plus Radioisotope Method Compared With the Radioisotope-Only Method for Breast Cancer Patients After Neoadjuvant Chemotherapy: A Prospective, Randomized, Open-Label, Single-Center Phase 2 Trial. Ann Surg Oncol. 2019 Aug;26(8):2409-2416. doi: 10.1245/s10434-019-07400-0. Epub 2019 May 7. PMID: 31065958

9. Jung SY, Kim SK, Kim SW, Kwon Y, Lee ES, Kang HS, Ko KL, Shin KH, Lee KS, Park IH, Ro J, Jeong HJ, Joo J, Kang SH, Lee S. Comparison of sentinel lymph node biopsy guided by the multimodal method of indocyanine green fluorescence, radioisotope, and blue dye versus the radioisotope method in breast cancer: a randomized controlled trial. Ann Surg Oncol. 2014 Apr;21(4):1254-9. doi: 10.1245/s10434-013-3437-0. Epub 2013 Dec 20. PMID: 24356798.

10. Kedrzycki MS, Leiloglou M, Ashrafian H, Jiwa N, Thiruchelvam PTR, Elson DS, Leff DR. Meta-analysis Comparing Fluorescence Imaging with Radioisotope and Blue Dye-Guided Sentinel Node Identification for Breast Cancer Surgery. Ann Surg Oncol. 2021 Jul;28(7):3738-3748. doi: 10.1245/s10434-020-09288-7. Epub 2020 Nov 6. PMID: 33156466; PMCID: PMC8184731.

11. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021 May;71(3):209-249. doi: 10.3322/caac.21660. Epub 2021 Feb 4. PMID: 33538338.

12. Thongvitokomarn S, Polchai N. Indocyanine Green Fluorescence Versus Blue Dye or Radioisotope Regarding Detection Rate of Sentinel Lymph Node Biopsy and Nodes Removed in Breast Cancer: A Systematic Review and Meta-Analysis. Asian Pac J Cancer Prev. 2020 May 1;21(5):1187-1195. doi: 10.31557/APJCP.2020.21.5.1187. PMID: 32458621; PMCID: PMC7541884.

13. Wang P, Shuai J, Leng Z, Ji Y. Meta-analysis of the application value of indocyanine green fluorescence imaging in guiding sentinel lymph node biopsy for breast cancer. Photodiagnosis Photodyn Ther. 2023 Sep; 43:103742. doi: 10.1016/j.pdpdt.2023.103742. Epub 2023 Aug 9. PMID: 37567333.

14. Wang C, Tong F, Cao Y, Liu P, Zhou B, Liu H, Cheng L, Liu M, Guo J, Xie F, Yang H, Wang S, Peng Y, Wang S. Long-term follow-up results of fluorescence and blue dye guided sentinel lymph node biopsy in early breast cancer. Breast Cancer Res Treat. 2021 Jul;188(2):361-368. doi: 10.1007/s10549-021-06196-6. Epub 2021 Mar 24. PMID: 3376

15. Xu Y, Yuan S, Chen M, Gong K, Liu Y, Li S, Xiong F, Pan Y, Cao J, Gong J, Luo N. Evaluation of indocyanine green combined with methylene blue staining in sentinel lymph node biopsy of breast cancer. Gland Surg. 2022 Sep;11(9):1489-1496. doi: 10.21037/gs-22-434. PMID: 36221275; PMCID: PMC9547706.