ORIGINAL ARTICLE

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Survival of patients with malignant neoplasms to be screened as part of the adult medical examination during the COVID-19 pandemic

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ABSTRACT

Purpose of the study. To assess the variations of survival in malignant neoplasms subject to screening as part of the regular adult population check-up (index MN, iMN) during the COVID-19 pandemic according to the data of the Arkhangelsk Regional Cancer Registry (ARCR).

Materials and methods. Data on nine iMN in the Arkhangelsk region were extracted from the ARCR database. Using the actuarial method, 1-year cancer-specific (CSS) and overall (OS) survival were estimated during the COVID-19 pandemic in 2020−2021. This period was compared with the 2018−2019 period before the pandemic. Differences between the periods were assessed using the log-rank method. Cox regression analysis was used to identify possible causes of differences in survival between the periods.

Results. A total of 12,354 records of nine iMNs were selected to analyze the survival during the COVID-19 pandemic. For all malignant neoplasms, there was a decrease in the one-year OSR rates, which was statistically significant for lung cancer (from 42.4 % to 32.8 %, $p = 0.0001$) and cervical cancer (from 90.3 % to 80.8 %, $p = 0.02$), and OS (by 2.6 %−11.0 %, significant for seven of the nine iMNs). Compared with the pre-COVID period, during the pandemic, the proportion of deaths of patients with iMNs from respiratory diseases increased by 1.5 times and the proportion of deaths from external causes increased from 3 % to 9 %, chi-square (4) = 41.8, $p = 0.00001$. In the regression models of CSS and OS, after adjusting for stage, the hazard ratio decreased from 1.15 (95 % confidence interval (CI) 1.07−1.24) to 1.10 (95 % CI 1.03−1.19) and from 1.22 (95 % CI 1.14−1.31) to 1.18 (95 % CI 1.10−1.26). In multivariable regression, the risk of cancer-specific and all-cause death in patients with malignant neoplasms during the pandemic remained higher by 16 % and 24 %.

Conclusion. The 15−33 % higher risk of cancer-specific and all-cause death during the COVID-19 pandemic is explained by an increase in the proportion of advanced stages due to limited access to screening. Longer-term survival analysis is required.

Keywords: adult population regular check-up, cancer screening, COVID-19 pandemic, causes of death of patients with malignant neoplasms, survival

Выживаемость больных злокачественными новообразованиями, подлежащих скринингу в рамках диспансеризации взрослого населения, во время пандемии COVID-19

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РЕЗЮМЕ

Цель исследования. Оценка динамики выживаемости при злокачественных новообразованиях, подлежащих скринингу в рамках диспансеризации взрослого населения (индексных злокачественных новообразований (иЗНО)), в период пандемии COVID-19 по данным Архангельского областного канцер-регистра (АОКР).

Материалы и методы. Из базы данных АОКР были извлечены сплошные данные о девяти иЗНО в Архангельской области. С помощью актуарного метода оценивали 1-летнюю опухолеспецифическую (ОСВ) и общую выживаемость (ОВ) в период пандемии COVID-19 в 2020–2021 гг. Этот период сравнивали с периодом 2018–2019 гг. до пандемии. Различия между периодами оценивали с помощью лог-рангового метода. Для выявления возможных причин различий в выживаемости между периодами применяли регрессионный анализ Сох.

Результаты. Всего для анализа динамики выживаемости в период пандемии COVID-19 было отобрано 12 354 записи о девяти иЗНО. При всех иЗНО произошло снижение показателей одногодичной ОСВ, статистически значимое при раке легкого (с 42,4 % до 32,8 %, p = 0,0001) и шейки матки (с 90,3 % до 80,8 %, p = 0,02), и ОВ (на 2,6–11,0 %, значимое у семи из девяти иЗНО). Сравнительно с доковидным периодом, в период пандемии возросла в 1,5 раза доля смертей больных иЗНО от заболеваний легких и с 3 % до 9 % доля смертей от внешних причин, хи-квадрат (4) = 41,8, p = 0,00001. В регрессионных моделях ОСВ и ОВ после поправки на стадию отношение рисков уменьшилось с 1,15 (95 % доверительный интервал (ДИ) 1,07–1,24) до 1,10 (95 % ДИ 1,03–1,19) и с 1,22 (95 % ДИ 1,14–1,31) до 1,18 (95 % ДИ 1,10–1,26). В многофакторной регрессии риск смерти от рака и от всех причин у больных иЗНО в период пандемии оставался на 16 % и 24 % более высоким.

Заключение. Повышенный риск смерти от рака и всех причин в период пандемии COVID-19 на 15–33 % объясняется увеличением доли распространенных стадий вследствие ограниченного доступа к скринингу. Требуется анализ выживаемости в более отдаленном периоде.

Ключевые слова: диспансеризация взрослого населения, скрининг рака, пандемия COVID-19, причины смерти больных ЗНО, выживаемость

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BACKGROUND

The medical regular check-up of the adult population was introduced in Russia in 2013, its main goal is to reduce mortality from non-communicable diseases through their primary prevention and screening [1]. Colorectal cancer, breast cancer, lung cancer, cervical cancer, and prostate cancer are among the oncological diseases to be screened as part of a medical examination [2–5]. At the initial stages of medical examination, cancers of the uterus, ovaries, and kidneys were also among the screened diseases [1].

Earlier, population analysis showed that after the introduction of the check-up, the incidence of more early cancers increased in most index malignancies [6] and patient survival improved [7]. Mortality rates from iMNs had a pronounced downward trend [8].

The COVID-19 pandemic has caused significant changes in the organization of cancer care and check-up. In March 2020, the check-up was temporarily suspended [9]. Special conditions were created for those who wanted to undergo a medical examination at this time, including a separate entrance and the opportunity to avoid visiting the registry. In countries with a long history of population-based screening, the decrease in the number of studies used for screening ranged from 51 % to 77 %, according to the meta-analysis [10]. The suspension of screening led to a catastrophic decrease in the proportion of early stages in most cases, especially in cervical cancer [11, 12], as well as to a decrease in the incidence, or rather, detectability, in most cancers [13].

Purpose of the study was to evaluate the dynamics of survival in case of iMN during the COVID-19 pandemic according to the Arkhangelsk Regional Cancer Registry (ARCR).

MATERIALS AND METHODS

The study received an approval No. 04/05-16 by the Ethics Committee of the Northern State Medical University dated 05/24/2016.

The Arkhangelsk Regional Cancer Registry (ARCR) has been continuously recording patients with MNs since 2000. The quality of the registry data (completeness, timeliness, reliability) has been confirmed by the results of international [14, 15] and domestic audits [16].

Index values. Taking into account the screening conditions within the check-up, cancers of the colon (International Classification of Diseases code 10 revision C18), rectosigmoid junction, rectum (C19, C20), trachea, bronchi and lung (C33, C34), breast (C50), cervix (C53), and uterine body were selected as the best (C54), ovaries (C56, C57), prostate (C61), kidneys (C64).

In August 2024, depersonalized data was extracted from the ARCR database to analyze the survival rate for each of the nine iMNs, for the period from 2018 to 2021. For the analysis, variables were used, including the identification number, full date of birth, gender, place of residence (city or village) of the patient, date of diagnosis, morphological code and topography of the tumor according to ICD-10, as well as the stage of the disease according to the classification of TNM UICC 8th edition, 2017.

Methods of analysis. The actuarial method was used to evaluate the 1-year cancer-specific (CSS) and overall survival (OS) during the COVID-19 pandemic in 2020–2021. This period was compared with the period 2018–2019 before the pandemic. The differences between the periods were assessed using the log-rank method. Cox regression analysis was used to identify possible causes of differences in survival between periods [17]. At the first stage of the analysis, the stage was introduced into the regression model of the one-year CSS and OS as an indicator of check-up cancellation during the pandemic, at the second stage all available variables were introduced. All calculated survival rates were presented with 95 % confidence intervals (95 % CI).

STUDY RESULTS

In total, 12,354 records of nine iMN cases were selected to analyze the dynamics of survival during the COVID-19 pandemic. Of these, 892 cases were accounted for posthumously, and therefore they were excluded from the analysis. The final survival analysis included 11,462 observations. At the time of the start of the survival analysis, 3133 (27 %) had died. The data on the studied localizations are presented in Table 1.

In general, with all the iMNs, there was a decrease in the indicators of the one-year CSS (Fig. 2).

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A statistically significant decrease in CSS rates occurred in lung cancer (from 42.4 % to 32.8 %, p = 0.0001) and cervical cancer (from 90.3 % to 80.8 %, p = 0.02). In cancer of the colon, rectum, uterus, ovaries, prostate, kidney, the decrease in CSS by 2.5 %–7.3 % did not reach statistical significance. In breast cancer, the CSS index did not change significantly during the pandemic. The dynamics of the one-year OS is shown in the Fig. 3.

OS indicators during the pandemic period decreased for all iMNs by from 2.6 % for breast cancer to 11.0 % for ovarian cancer, the differences are statistically significant for seven out of nine iMNs. The structure of mortality from causes unrelated to index cancer has changed. From other causes, 726 patients died in 2018–2019, and 445 patients died in 2020–2021. Compared with the pre-epidemic period, the proportion of deaths from lung diseases increased 1.5 times during the pandemic and the proportion of deaths from external causes increased from 3 % to 9 %, chi-squared (4) = 41.8, p = 0.00001 (Fig. 4).

Table 1. Patients with iMN in AR for survival analysis in the periods 2018−2019 and 2020−2021. ARCR Data

Topography ICD-3	Total number of registered in 2018–2021 DB	Accounted after death, n (%)	Included in the survival rate analysis	iMN deaths during the analysis (out of included in the analysis), n (%)
C18	1821	153 (8 %)	1668	566 (34 %)
C19-20	1173	75 (6 %)	1098	340 (31 %)
C34	2314	321 (14 %)	1993	1316 (66 %)
C50	2089	45 (2 %)	2044	201 (10 %)
C53	696	11 (2 %)	685	120 (18 %)
C54	802	27 (3 %)	775	106 (14 %)
C56-57	558	34 (6 %)	524	142 (27 %)
C61	1922	110 (6 %)	1812	175 (10 %)
C64	979	116 (6 %)	863	167 (19 %)
Overall	12354	892 (7 %)	11462	3133 (27 %)

Note: hereafter, the codes and iMNs for the international classification of diseases 10 are: C18 – colon, C19-20 – rectosigmoid junction, rectum, C33-34 – trachea, bronchi and lung, C50 – mammary gland, C53 – cervix, C54 – uterine body, C56-57 – ovaries, C61 – prostate gland, C64 – kidneys
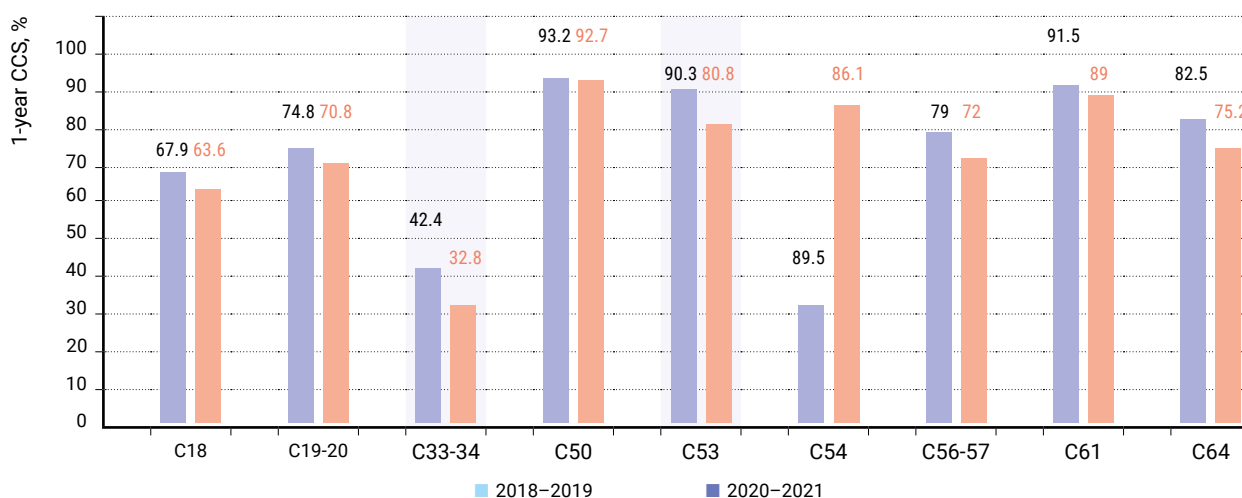
Fig. 1. Dynamics of one-year cancer-specific survival rates in the periods 2018−2019 and 2020−2021. ARCR data. The boxes show statistically significant differences

Among them, the most significant increase in the proportion of deaths from diseases of the respiratory system occurred in patients with cancer of the rectum (from 21 % to 38 %, *p* = 0.08), lung (from 11 % to 38 %, *p* < 0.0001), breast (from 25 % to 32 %, *p* = 0.009), uterus body (from 11 % to 35 %, *p* = 0.03). In prostate and kidney cancers, the proportion of deaths from lung diseases did not increase.

The results of the regression analysis of OS and CSS are presented in the Tables 3 and 4.

During the COVID-19 pandemic, the risk of death from cancer during the first year after the establishment of the iMN increased by 15 %, *p* = 0.0002, compared with the nearest previous period in 2018−2019. The correction for the stage (the effect of the cancellation of the medical examination) reduced the risk ratio to 1.10, *p* < 0.0001; in the multiple regression, after adjusting for all the factors available in the register, the HR returned to the initial value, the
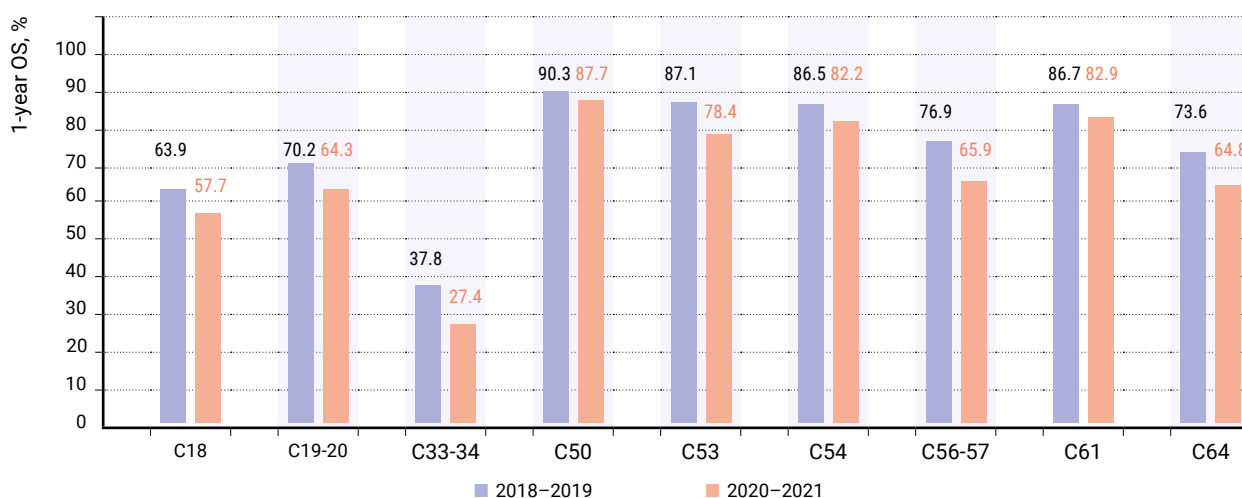

Fig. 2. Dynamics of one-year overall survival rates in the periods 2018−2019 and 2020−2021. ARCR data. The boxes show statistically significant differences
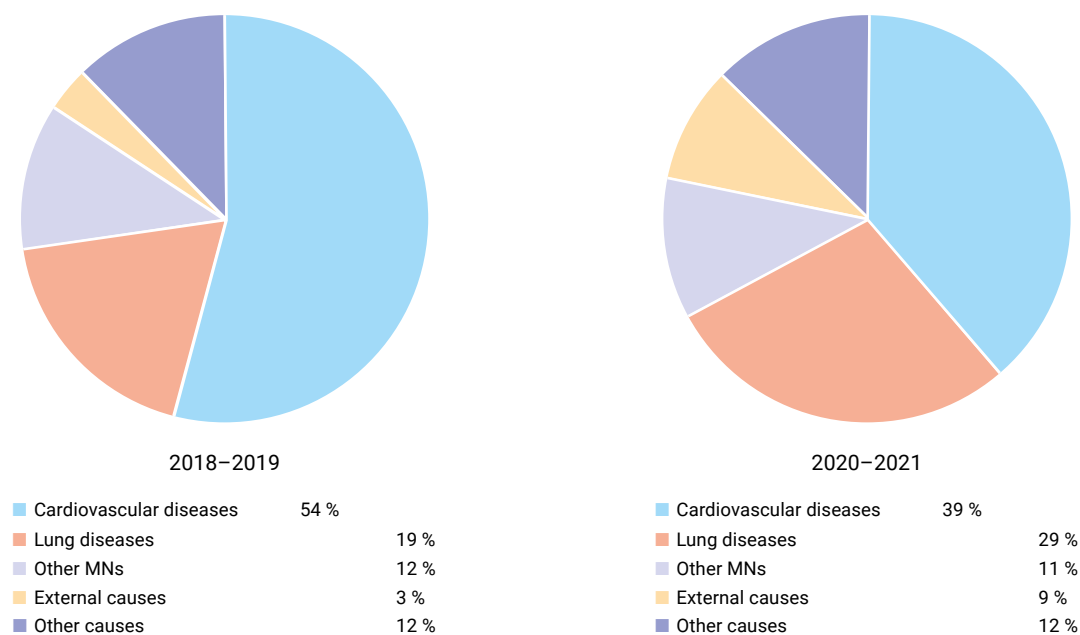

Fig. 3. The structure of mortality from other causes of iMN in the periods 2018−2019 and 2020−2021

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differences between the periods, $p < 0.0001$. Among individual patients, a significant increase in the risk of cancer death during the pandemic occurred in lung cancer (HR = 1.24, p = 0.0002) and cervical cancer (HR = 1.60, p = 0.02). The correction for stage left significant differences for lung cancer; in multiple regression, the risk of death from iMN was significantly higher for colon and lung cancers.

The risk of death from any cause with iMN during the pandemic was 15–52 % higher than in the previous period, and for seven out of nine iMN it was statistically significant. The stage adjustment left a significant higher risk of death for colon, lung, and prostate cancers. The COVID-19 pandemic remained an independent factor of unfavorable prognosis in multiple regression in all cases, with the exception of breast, cervical, and uterine cancers.

Table 2. Results of the Cox regression analysis of the 1-year CSS with iMN compared to the data obtained in the periods of 2018−2019 and 2020−2021. ARCR Data

Topography ICD-3	1-year CSS, death risk ratio for the period 2020−2021 compared with the reference period 2018−2019 (95 % CI)		
	Model 1 one-factor analysis	Model 2 stage correction	Model 3 multifactorial
C18	1.05 (0.89−1.26)	1.08 (0.91−1.30)	1.26 (1.06−1.51)
C19-20	1.22 (0.96−1.54)	1.06 (0.84−1.35)	1.20 (0.95−1.52)
C33-34	1.24 (1.11−1.39)	1.17 (1.05−1.32)	1.12 (1.01−1.26)
C50	1.09 (0.79−1.52)	1.01 (0.73−1.41)	1.04 (0.75−1.45)
C53	1.60 (1.08−2.37)	1.15 (0.78−1.71)	1.19 (0.80−1.78)
C54	1.32 (0.88−1.98)	1.35 (0.89−2.05)	1.18 (0.78−1.81)
C56-57	1.26 (0.88−1.79)	1.18 (0.83−1.70)	1.28 (0.89−1.86)
C61	1.24 (1.10−1.76)	1.30 (1.02−1.65)	1.11 (0.79−1.53)
C64	1.23 (0.89−1.71)	1.04 (0.75−1.45)	1.37 (0.98−1.94)
All iMNs	1.15 (1.07−1.24)	1.10 (1.03−1.19)	1.16 (1.08−1.26)

Table 4. The results of the regression analysis of the 1-year OS with iMN in comparison with the data obtained in the periods of 2018−2019 and 2020−2021. ARCR Data

Topography ICD-3	1-year OS, death risk ratio for the period 2020−2021 compared with the reference period 2018−2019 (95 % CI)		
	Model 1 one-factor analysis	Model 2 stage correction	Model 3 multifactorial
C18	1.15 (0.98−1.34)	1.19 (1.01−1.39)	1.38 (1.17−1.62)
C19-20	1.29 (1.05−1.59)	1.15 (0.94−1.42)	1.32 (1.07−1.63)
C33-34	1.26 (1.14−1.40)	1.20 (1.08−1.34)	1.15 (1.03−1.28)
C50	1.33 (1.03−1.72)	1.26 (0.98−1.63)	1.25 (0.97−1.63)
C53	1.52 (1.07−2.16)	1.11 (0.78−1.58)	1.16 (0.81−1.66)
C54	1.44 (1.01−2.04)	1.38 (0.97−1.98)	1.21 (0.84−1.74)
C56-57	1.39 (1.00−1.93)	1.32 (0.95−1.84)	1.43 (1.02−2.01)
C61	1.40 (1.10−1.76)	1.30 (1.02−1.65)	1.32 (1.04−1.68)
C64	1.27 (0.96−1.69)	1.12 (0.84−1.49)	1.42 (1.06−1.91)
All iMNs	1.22 (1.14−1.31)	1.18 (1.10−1.26)	1.24 (1.16−1.33)

DISCUSSION

In our study conducted according to the ARCR data, we found a significant decrease in the rates of one–year OS in lung and cervical cancer, and one-year OS in seven out of nine cases. At the same time, for most of them, these changes were associated with a decrease in the proportion of early stages, which is naturally associated with limitations in conducting check-up. During the pandemic, the proportion of deaths from respiratory diseases increased by 48 % and from suicide tripled.

A statistically significant decrease in CSS indicators in our analysis was recorded in cases of pulmonary and cervical fever. It was for these types of cancer that in a previously published study according to the cancer registry of the Arkhangelsk region, we found the most significant decrease in the proportion of early stages among all of them – by 20–35 %. Moreover, there was also an increase in the proportion of neglected cases by 25 % in lung cancer, and the proportion of cervical cancer patients diagnosed in stages III and IV increased by 80 % and 30 %, respectively, compared with the pre-pandemic period [12].

Our data is consistent with the data of other authors. Thus, Barclay NL, et al. A population-based cohort study of electronic medical records of several common cancers from the UK National Database was conducted. A total of 12,259,744 patients aged ≥ 18 years with a history of cancer ≥ 1 year, detected from January 2000 to December 2022, were included. Short-term survival in many cancers was reduced, albeit minimally, during the period, while the decrease in survival in colorectal cancer was equivalent to a return to the mortality rate observed in the first decade of the 2000s. Although data on long-term survival is needed to fully understand the impact of COVID-19 on cancer treatment, the authors conclude that these results illustrate the need for urgent and significant action by the UK National Health Service to address the existing backlog in cancer screening and diagnosis procedures to improve cancer treatment and reduce mortality [18].

Adjusting for all the factors available in the registry database in our study led to a further increase in the value of the death risk ratio when comparing OS and OS during the pandemic compared with the pre-pandemic period. This may indicate that a higher risk of death is influenced not only by the high prevalence of heart disease at the time of diagnosis, but also by other important factors, including delayed diagnosis, lower availability of treatment, especially for elderly patients and during a pandemic.

These factors have been studied in a number of studies. Thus, in a meta-analysis, Tope P, et al. Comparable estimates of mortality risk were found for the time intervals from surgery to adjuvant chemotherapy for breast cancer, colorectal cancer, and ovarian cancer. Risk assessments of a complete pathological response indicated an optimal time window of 7–8 weeks for completion of neoadjuvant chemotherapy before surgery for rectal cancer [19], which, accordingly, could not be performed in absolutely all patients during the pandemic.

The advantage of our analysis is its population-based nature: we analyzed the outcomes of all patients with index-related iMNs registered in the Arkhangelsk region, which allows us to extrapolate the results obtained to the population of the entire country. The limitation of the study is also related to the type of study itself. The registry data, as a rule, does not include detailed information about the genetics and morphology of tumors, the condition of patients and the details of treatment. Therefore, the results of the analysis should be interpreted carefully.

The relatively short period that has passed since the pandemic does not allow us to draw definitive conclusions about the impact of COVID-19 on the survival rates of cancer patients. Further analyses are required in a more distant period of time.

CONCLUSION

Thus, the COVID-19 pandemic had a significant impact on the outcomes of treatment for iMNs. An increase in the initial prevalence and other pandemic-related factors led to a significant decrease in one-year OS by 10 % in lung and cervical cancers and one-year OS by 3–10 % in cancers of the rectum, lung, breast, cervix and uterus, ovaries and prostate. In most cases, the contribution of an unfavorable change in the stage distribution in the period 2020–2021 to the deterioration of the indicators of CSS and OS was significant. Further analysis of survival in a more distant period is required.

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