

ACCELERATED HIGH-TECH RADIOTHERAPY DURING THE COVID-19

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ABSTRACT

Relevance: COVID-19 impacts the course of cancer depending on the status and volume of cancer patient vaccination against COVID-19.

The study aimed to assess the impact of accelerated high-tech radiation therapy on the course of the oncological process, depending on the status and volume of COVID-19 vaccinations.

Methods: This quantitative and qualitative prospective randomized controlled scientific study was conducted as part of the implementation of the scientific project, "Innovative approach to managing patients with cancer in the context of the COVID pandemic-19," Reg. No. AP13068657. The study involved 221 cancer patients.

Results: COVID-19 was diagnosed in 54/221 (24.4%) of the study participants, 24 (22.4%) in the standard radiotherapy group, and 30 (26.3%) in the experimental radiotherapy group. 49/221 (22.2%) of the participants were vaccinated. COVID-19 was detected in one breast cancer patient in the experimental group (1.5%) two months after vaccination and two patients with prostate cancer (2.4%) four months after vaccination. Relapse-free survival was registered in 59 (85.5%) breast cancer patients in the standard group and 58 (85.3%) in the experimental group. The overall survival of breast cancer patients was 69 (100.0%) in the standard group and 68 (97.0%) in the experimental group. Relapse-free survival was registered in 32 (84.2%) prostate cancer patients in the standard group and 41 (89.1%) patients in the experimental group. The overall survival among prostate cancer patients was 34 (89.5%) in the standard group and 45 (97.8%) in the experimental group. The deaths were not related to COVID-19. The average treatment duration for breast cancer was less by 12.9 days, with prostate cancer— by 18.2 days.

Conclusion: In Kazakhstan, 4.8% of cancer patients with COVID-19 died in 2020-2021. The use of accelerated high-tech radiotherapy is justified in the context of the COVID-19 pandemic. Vaccination can prevent COVID-19 development in cancer patients.

Keywords: radiotherapy, pandemic, COVID-19, oncology, vaccination.

Introduction: At the end of 2019, China informed the World Health Organization (WHO) of a severe respiratory disease caused by SARS CoV-2 severe acute respiratory syndrome coronavirus 2 (COVID-19) [1]. This highly contagious infection with aerosol-droplet and household contact transmission mechanisms with damage to the lung tissue is induced by a new virus strain from the SARS-CoV-2 coronavirus genus [2].

In early March 2020, WHO declared a pandemic due to the rapid global spread of this infection [3]. COVID-19 pandemic restrictions have resulted in a dramatic time shift in cancer care, with hospitals reducing patient visits and implementing remote consultations and telemedicine, postponing elective surgeries, systemic chemotherapy and radiotherapy (RT), elective dispensary supervision, and internal consultations [4]. Unfortunately, epidemiological indicators suggest this pandemic will continue for years [5].

According to global studies, cancer patients are at higher risk of contracting COVID-19 [6]. In addition, the guidelines of the professional oncology communities generally recommend changes in the practice of specific anticancer therapy to minimize immune compromise effects that may predispose to serious complica-

tions during a pandemic [7]. According to a nationwide study in China, receiving chemotherapy or surgery during COVID-19 infection was associated with a higher risk of symptomatic and severe COVID-19 in cancer patients compared with patients who did not receive chemotherapy or surgery (75 % versus 43%, $p=0.0026$) [8]. However, a delay in specialized treatment usually results in the deterioration of the patient's condition and the disease progression. At delayed chemotherapy and surgery, RT may play an even more important role in treating most cancers, as RT is one of the few specific treatments that can be safely used with little impact on the immune system [9, 10].

Patients receiving RT usually require a multi-fractional course of treatment. RT cannot be delayed like other treatments without the risk of adverse clinical consequences [11]. During the COVID-19 pandemic, modern methods of radiation therapy continue to be used in the treatment process: intensively modulated radiation therapy (IMRT), volumetric-modulated arc therapy (VMAT), and image-guided radiation therapy (IGRT) [12]. In the context of limited resources during the COVID-19 pandemic, it is necessary to minimize the number of patient visits to a medical facility while

maintaining an identical biologically effective dose, which allows for expanding the possibilities of RT [13].

COVID-19 impacts the course of cancer depending on the status and volume of vaccination of cancer patients against COVID-19. However, the authors could find no published results of RT in cancer patients during the COVID-19 pandemic in the Republic of Kazakhstan.

The study aimed to assess the impact of accelerated high-tech radiation therapy on the course of the oncological process, depending on the status and volume of COVID-19 vaccinations.

Materials and Methods: This quantitative and qualitative prospective randomized controlled scientific study was conducted as part of the implementation of the scientific project of the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan under the calendar plan for 2022 of the scientific project, "Innovative approach to managing patients with cancer in the context of the COVID pandemic-19," Reg. No. AP13068657.

The study involved 114 cancer patients who were administered an RT course by multidisciplinary group decision and a control group of 107 cancer patients. All the patients have signed an informed consent to participate in the study. Patients were randomized by an envelope method in a ratio of 1 to 1 in the experimental and standard radiotherapy groups. Tools for summarizing and grouping materials, compiling and analyzing databases for statistical processing, and visualizing the data obtained were used Microsoft Excel programs and the IBM SPSS Statistics 21 package (trial version). According to the information systems of the Electronic Register of Cancer patients (EROB), the Electronic Register of Inpatients (ERSB), and the medical information system "DamuMed" in cancer patients under dynamic observation, an assessment was made of the status of vaccination against COVID-19, the type of vaccine, its dosage, vaccination period relative to the start or interruption of specialized treatment, relapse-free, and overall survival and the course of the oncological process. Identification of determinants and risk factors of radiation therapy: age, concomitant diseases of the heart and lung system, diabetes mellitus, hormonal therapy, chemotherapy, and body mass index. The determinants for successful RT depended on the RT method.

Results: Despite a certain improvement in COVID-19 epidemiological situation in Kazakhstan, in 2021, 18,502 cancer patients contracted COVID, accounting for 9.5% of cancer patients under dynamic observation (194,510 people). Of them, 898 died from COVID-19, amounting to 0.5% of patients under dynamic observation and 4.5% of those with COVID-19. In 2020, only 4,518 patients contracted COVID-19 (2.4% of those under observation); 199 died from COVID-19 (0.1% of those under observation and 4.4% of those with COVID-19). In 2020-2021, 23,020 cancer patients fell ill with COVID-19, and 1,097 cancer patients died (4.8% of those with COVID-19).

In compliance with the ethical principles reflected in the Helsinki Declaration of Patient Safety ("Ethical

principles for medical research involving a human as a subject," as amended by the 64th WMA General Assembly. – Fortaleza, Brazil, 2013), and in accordance with the law Republic of Kazakhstan, 221 patients were recruited: 137 of them were diagnosed with breast cancer and 84 patients with prostate cancer. Of them, 114 patients received experimental high-tech radiation therapy (68 patients with breast cancer and 46 patients with prostate cancer), a control group of 107 patients (69 patients with breast cancer and 38 patients with prostate cancer) who received high-tech radiotherapy techniques in the standard mode. In both groups, treatment was carried out on a linear electron accelerator from Varian, USA, "TrueBeam," 5 fractions per week under daily control of imaging systems (IGRT) with a comparison of soft tissues and bone structures. The data obtained during the study are subject to the law of normal distribution of data, parametric tests for statistical analysis are used, and a probability of 95% is determined to eliminate the systematic error of the study.

In total, COVID-19 was detected in 54/221 (24.4%) patients included in the study, 24 patients (22.4%) in the standard radiotherapy group, and 30 patients (26.3%) in the experimental radiotherapy group. 49/221 (22.2%) patients in the study group were vaccinated. At the same time, COVID-19 was detected only in 1 breast cancer patient in the experimental radiotherapy group (1.5%) 2 months after she was vaccinated. And COVID-19 was detected in two prostate cancer patients (2.4%) four months after vaccination on average: in one (2.6%) prostate cancer patient one month after vaccination in the standard radiotherapy group, and one (2.2%) prostate cancer patient six months after vaccination in the experimental radiotherapy group.

When analyzed by location, COVID-19 was detected in 32 breast cancer patients (23.4%). Of these, 14 patients (20.3%) were in the standard radiotherapy group, and 18 patients (26.4%) were in the experimental radiotherapy group. COVID-19 was detected in 22 patients with prostate cancer (26.2%), ten patients (26.3%) in the standard radiotherapy group, and 12 patients (26.1%) in the experimental radiotherapy group.

Comparison of relapse-free and overall survival rates and the course of the oncological process: when analyzed by location, relapse-free survival was observed in 59 (85.5%) breast cancer patients in the standard radiotherapy group and 58 (85.3%) breast cancer patients in the experimental radiotherapy group. Overall survival was observed in 69 (100.0%) breast cancer patients in the standard radiotherapy group and 68 (97.0%) breast cancer patients in the experimental radiotherapy group. The deaths were not related to COVID-19.

Disease-free survival was observed in 32 (84.2%) prostate cancer patients in the standard radiotherapy group and 41 (89.1%) prostate cancer patients in the experimental radiotherapy group. Overall survival was observed in 34 (89.5%) prostate cancer patients in the standard radiotherapy group and 45 (97.8%) patients in the experimental radiotherapy group. The deaths were not related to COVID-19.

Discussion:

Patient follow-up will continue, but a clear advantage in the experimental RT group is that the average duration of treatment for breast cancer is less by 12.9 days, and for prostate cancer, it is less by 18.2 days. Reducing the number of radiation therapy sessions in the context of the COVID-19 pandemic and saving human and technical resources also reduces waiting times and increases the coverage of radiation therapy for cancer patients. The scientific and socio-economic impact of this scientific study gives impetus to the study of the problem of treating cancer patients in a pandemic and evaluates the results of experimental radiotherapy. The study's results will scientifically substantiate the redistribution of financial resources to increase efficiency in the budgetary financing of radiotherapy services from the state budget by reducing sessions per patient.

Conclusions: In 2020–2021, 23,020 cancer patients fell ill with COVID-19 in Kazakhstan, of which 1,097 cancer patients died from COVID-19, which accounted for 4.8% of those with COVID-19. The use of accelerated high-tech radiotherapy is justified to save human and technical resources, which reduces the queue and waiting time for radiotherapy for cancer patients in the context of the COVID-19 pandemic. Vaccination does not impair outcomes but rather prevents the development of COVID-19 in cancer patients.

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АНДАТПА**COVID-19 ПАНДЕМИЯ ЖАҒДАЙЫНДАҒЫ ЖЕДЕЛДЕТІЛГЕН ЖОҒАРЫТЕХНОЛОГИЯЛЫҚ СӘУЛЕЛІК ТЕРАПИЯ**

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Өзектілігі: Қазіргі уақытта вакцинация мәртебесі мен көлеміне және онкологиялық науқастарды COVID-19-ға қарсы вакцинациямен қамтуға байланысты COVID-19-дың онкологиялық аурудың ағымына әсері туралы деректер пайда болды.

Зерттеудің мақсаты: COVID-19-ға қарсы егілген екінің мәртебесі мен көлеміне байланысты онкологиялық процестің ағымына жеделдетілген жоғары технологиялық сәулелік терапияның әсер етуін бағалау.

Әдістері: Бұл сандық және сапалық перспективті рандомизацияланған бақыланатын ғылыми зерттеу «COVID-19 пандемиясы жағдайында онкологиялық науқастарды басқаруға инновациялық көзқарас» ғылыми жобасын іске асыру шеңберінде жүзеге асырылды, тіркеу нөмірі AP13068657.

Зерттеуге мультидисциплинарлық топтың шешімімен РТ курсы тағайындалған 114 онкологиялық науқастар және 107 онкологиялық науқастардың бақылау тобы қатысты.

Нәтижелері: жалпы зерттеуге қатысқан 221 пациенттің 54-де (24,4%), яғни стандартты сәулелік терапия тобындағы 24 пациентте (22,4%) және эксперименттік сәулелік терапия тобындағы 30 пациентте (26,3%) ғана COVID-19 анықталды. Зерттеуге қатысқан 221 пациенттің 49-на (22,2%) ғана екі егілді. Бұл ретте COVID-19 сырқаты екі егілгеннен кейін 2 ай өткен соң эксперименттік терапия (1,5%) тобындағы сүт безі қатерлі ісігімен ауыратын тек 1 пациентте ғана анықталды. Және қуық асты безінің қатерлі ісігімен ауыратын 2 пациентте екі егілгеннен кейін шамамен 4 айдан кейін COVID-19 анықталды. Сүт безі қатерлі ісігімен ауыратын стандартты терапия тобындағы пациенттердің рецидивсіз өмір сүруі 59 (85,5%) болса, эксперименттік терапия тобындағы пациенттерде рецидивсіз өмір сүру 58 (85,3%)-ды құрады. Сүт безі обьры пациенттерінің жалпы өмір сүру деңгейі стандартты терапия тобында 69 (100,0%) және эксперименттік терапия тобында 68 (97,0%). Қуықасты безі қатерлі ісігі пациенттерінің рецидивсіз өмір сүруі стандартты терапия тобында 32-де (84,2%) және эксперименттік терапия тобында 41-де (89,1%) пациентте байқалды. Қуық асты безінің қатерлі ісігі науқастарының жалпы өмір сүру деңгейі стандартты терапия тобында 34 (89,5%) және эксперименттік терапия тобында 45 (97,8%) құрайды. Өлім-жітім жасадайлары COVID-19-бен байланысты емес. Жеделдетілген жоғары технологиялық сәулелік терапиямен Сүт безі қатерлі ісігін емдеудің орташа ұзақтығы 12,9 күн, ал қуықасты безінің қатерлі ісігін емдеудің ұзақтығы 18,2 күнге аз болады.

Корытынды: Қазақстанда COVID-19-бен 23020 онкологиялық науқас ауырды, оның ішінде 2020-2021 жылдары 1097 (4,8%) пациент қайтыс болды. Жеделдетілген жоғары технологиялық сәулелік терапияны қолдану COVID-19 пандемиясы жағдайында негізделген. Екпе егу онкологиялық науқастарда COVID-19 дамуын болдырмауға мүмкіндік береді.

Түйінді сөздер: сәулелік терапия, пандемия, COVID-19, онкология, вакцинация.

АННОТАЦИЯ

УСКОРЕННАЯ ВЫСОКОТЕХНОЛОГИЧНАЯ ЛУЧЕВАЯ ТЕРАПИЯ В УСЛОВИЯХ ПАНДЕМИИ COVID-19

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Актуальность: В настоящее время появились данные по влиянию COVID-19 на течение онкологического заболевания в зависимости от статуса и объема вакцинирования и охват онкологических больных вакцинацией против COVID-19.

Цель исследования – оценить влияние ускоренной высокотехнологичной лучевой терапии на течение онкологического процесса в зависимости от статуса и объема вакцинирования против COVID-19.

Методы: Данное количественное и качественное проспективное рандомизированное контролируемое научное исследование проведено в рамках реализации научного проекта «Инновационный подход к ведению онкобольных в условиях пандемии COVID-19», рег. номер AP13068657.

В исследовании приняли участие 114 онкологических больных, которым по решению мультидисциплинарной группы был назначен курс ЛТ, и контрольной группы из 107 онкологических больных.

Результаты: Всего COVID-19 был выявлен у 54 (24,4%) из 221 пациента, вошедших в исследование, в том числе у 24 пациентов (22,4%) в группе стандартной лучевой терапии и 30 пациентов (26,3%) в группе экспериментальной лучевой терапии. Всего 49 (22,2%) из 221 участника исследования были вакцинированы. При этом COVID-19 был выявлен только у 1 пациентки РМЖ в группе экспериментальной терапии (1,5%) через 2 месяца после вакцинации. И COVID-19 был выявлен у 2 пациентов РПЖ (2,4%) в среднем через 4 месяца после того, как они были вакцинированы. Безрецидивная выживаемость пациентов РМЖ у 59 (85,5%) в группе стандартной терапии и у 58 (85,3%) в группе экспериментальной терапии. Общая выживаемость пациентов РМЖ 69 (100,0%) в группе стандартной терапии и 68 (97,0%) в группе экспериментальной терапии. Безрецидивная выживаемость пациентов с РПЖ наблюдалась у 32 (84,2%) в группе стандартной терапии и у 41 (89,1%) в группе экспериментальной терапии. Общая выживаемость пациентов РПЖ составила 34 (89,5%) в группе стандартной терапии и 45 (97,8%) в группе экспериментальной терапии. Случаи смерти не были связаны с COVID-19. Средняя продолжительность курса лечения при РМЖ была меньше на 12,9 дней, при РПЖ – меньше на 18,2 дня.

Заключение: В Казахстане за 2020-2021 гг. умерли 4,8% онкологических больных, заболевших COVID-19. Использование ускоренной высокотехнологичной лучевой терапии обосновано в условиях пандемии COVID-19. Вакцинация позволяет предотвратить развитие COVID-19 у онкологических больных.

Ключевые слова: лучевая терапия, пандемия, COVID-19, онкология, вакцина.

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