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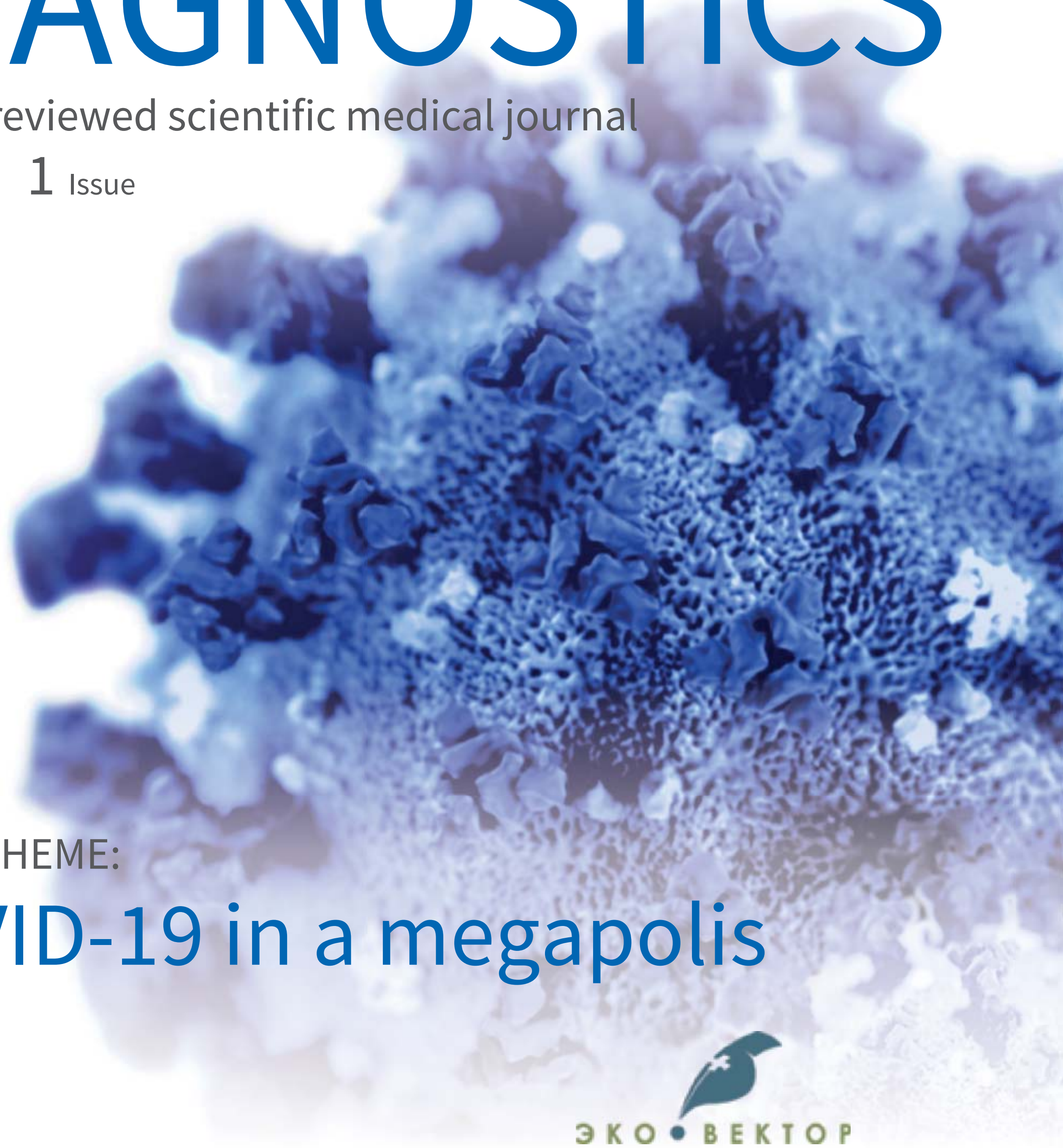

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Мобилизация научно-практического потенциала службы лучевой диагностики г. Москвы в пандемию COVID-19

© С.П. Морозов[1], Е.С. Кузьмина[1], Н.В. Ледихова[1], А.В. Владзимирский[1], И.А. Трофименко[1], О.А. Мокиенко[1], Е.В. Панина[1], А.Е. Андрейченко[1], О.В. Омелянская[1], В.А. Гомболевский[1], Н.С. Полищук[1], И.М. Шулькин[1], Р.В. Решетников[1, 2*]

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Уже в начале первой волны пандемии COVID-19 для компьютерной томографической (КТ) диагностики поражения лёгких у пациентов с подозрением на вирусную пневмонию в Москве была сформирована сеть амбулаторных КТ-центров (АКТЦ) с круглосуточным режимом работы. Введение шкалы «КТ 0-4» позволило проводить эффективную маршрутизацию. Для предотвращения распространения инфекции среди пациентов и персонала было введено зонирование АКТЦ с разбиением на «красную», «буферную» и «зелёную» зоны. В рамках мобилизации службы лучевой диагностики создан Московский референс-центр, осуществляющий контроль качества, экспертные дистанционные консультации и организационно-методическое сопровождение. Разработано несколько дистанционных курсов и обучающих вебинаров. Для распознавания признаков COVID-19 и оценки степени тяжести были подключены сервисы искусственного интеллекта. Разработанная стратегия службы лучевой диагностики г. Москвы обеспечила готовность к высокой нагрузке на систему здравоохранения города и позволила минимизировать потери среди медицинского персонала. Специалисты службы внесли существенный вклад в эффективное сдерживание распространения инфекции за счёт доступной, своевременной и качественной диагностики и маршрутизации.

Ключевые слова: КТ; COVID-19; искусственный интеллект.

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Mobilizing the academic and practical potential of diagnostic radiology during the COVID-19 pandemic in Moscow

Sergey P. Morozov[1], Ekaterina S. Kuzmina[1], Natalya V. Ledikhova[1], Anton V. Vladzymyrskyy[1], Irina A. Trofimenko[1], Olesya A. Mokienko[1], Elena V. Panina[1], Anna E. Andreychenko[1], Olga V. Omelyanskaya[1], Victor A. Gombolevskiy[1], Nikita S. Polishchuk[1], Igor M. Shulkin[1], Roman V. Reshetnikov[1, 2*]

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At the beginning of the first wave of the COVID-19 pandemic, a network of outpatient CT centers (OCTC) for lung pathology diagnostics in patients with suspected viral pneumonia with the round-the-clock operation was formed in Moscow. The introduction of the "CT 0-4" scale allowed for effective routing. To prevent the spread of infection among patients and staff, OCTC zoning was introduced, dividing into "red," "buffer," and "green" zones. As part of the mobilization of the Radiology Service, the Moscow Reference Center was established, aimed at quality control, remote expert consultations, and organizational and methodological support. Several online courses and training webinars have been developed. Artificial Intelligence services were connected to recognize the signs of COVID-19 and assess the severity.
The developed strategy of the Moscow Radiology Service ensured readiness for the high burden on the city health care system and minimized losses among medical personnel. The experts significantly contributed to effective infection control through accessible, timely, and high-quality diagnostics and routing.

Keywords: CT; COVID-19; artificial intelligence.

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调动莫斯科辐射诊断服务处在COVID-19大流行中的科学和实际潜力

Sergey P. Morozov[1], Ekaterina S. Kuzmina[1], Natalya V. Ledikhova[1], Anton V. Vladzymyrskyy[1], Irina A. Trofimenko[1], Olesya A. Mokienko[1], Elena V. Panina[1], Anna E. Andreychenko[1], Olga V. Omelyanskaya[1], Victor A. Gombolevskiy[1], Nikita S. Polishchuk[1], Igor M. Shulkin[1], Roman V. Reshetnikov[1, 2*]

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在2019冠状病毒第一波大流行开始之际，莫斯科已经建立了一个24小时运转的门诊CT诊断中心，用于对疑似病毒性肺炎患者肺部损伤的计算机断层扫描（CT）诊断。CT0—CT4量表的引入允许高效路由。为防止感染在患者和工作人员之间的传播，门诊CT中心被分为《红色》、《缓冲》和《绿色》区。作为辐射诊断服务动员的一部分，成立了莫斯科基准中心，进行质量控制、专家远程咨询以及组织和方法支助。还编制了几个远程学习课程和网络讨论会。人工智能服务被用于识别COVID-19的迹象和评估疾病的严重程度。莫斯科辐射诊断服务处制定的战略确保为该市医疗系统的高负荷做好准备，并使医务人员的死亡率降至最低。该服务处的专家通过可达性、及时和高质量的诊断和路由，为有效遏制疫情传播作出了重大贡献。

关键词：计算机断层扫描；COVID-19；人工智

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Moscow — a large and busy metropolis with an extensive network of airports—will always remain at the center of any outbreak of an infectious disease. It is not surprising that 26% of all reported coronavirus disease (COVID-19) cases in Russia is accounted for Moscow [1], which secured its position among the cities with the highest rates of COVID-19 cases[1]. However, Moscow's first-hand experience in managing the outbreak is, in its own way, distinctive. During the first wave, the peak incidence of 53 cases per 100,000 people was registered on May 7, 2020 [1], although the strict lockdown was announced only on March 29, 2020[2]. To put this into perspective, in large cities of Spain, Germany, Italy, and USA, the period between the introduction of lockdown measures and the surge in COVID-19 cases was 12 ± 3 days[3] [2–4]. Such a slowdown can largely be associated with the agents of Moscow Health Care Department who developed and implemented national action plans, where the primary care sector played the pivotal role.

The key goals of the health care system during any pandemic are to limit disease spread and reduce case fatality rates. For this reason, only patients with objectively severe condition are hospitalized, whereas patients with asymptomatic COVID-19 who are capable of managing their illness at home are quarantined. Failure to do so could overload the national health care system, which could negatively affect the quality of health services and propagate adverse treatment outcomes.

Diagnostic tests that detect viral RNA based on reverse-transcription polymerase chain reaction (RT-PCR) are considered as reference standards for the diagnosis of COVID-19. However, this method has low sensitivity [5], the testing process is slow, the RT-PCR testing for severe acute respiratory syndrome coronavirus 2 has high false-negative rate [6], and the availability and quality of reagents are critical for successful testing. For example, the shortage in viral RNA isolation kits became a major problem of laboratories worldwide[4]. Moreover, although RT-PCR testing helps determine disease severity by measuring the viral load [7], the diagnosis is established exclusively by the presence of either positive or negative test results. This disadvantage adds to the overall lack of clinical information.

One of the most common COVID-19 symptoms is viral pneumonia [8]. Computed tomography (CT) of the chest, though not known as a conventional modality in the diagnosis of acute respiratory virus infections, is very sensitive in examining for the presence of consolidations in the lungs–a typical sign of COVID-19. In light of this, the Moscow Radiology Department developed and introduced a strategy (Fig. 1) that revolved around the concept of a "clinically confirmed COVID-19 case".

This concept offers the criteria for COVID-19 diagnosis, which include a combination of symptoms typical for acute respiratory infection and presence of distinct patterns in the lungs. To measure the consolidation area, the clinicians developed an empirical visual scale "CT 0–4," which consists of five grades [9]. Here, CT-0 is assigned to patients who do not manifest pneumonia symptoms, while the remaining grades differ from one another by the size of the consolidation, each being 25% bigger than the previous. As the pandemic passes, chest CT has become a major component of COVID-19 diagnostics.

The introduction of the "CT 0–4" scale contributed to improving the triage process: while patients presenting with CT-0, CT-1, and CT-2 grades are managed at home with the assistance of telemedicine technologies, those with severe condition required immediate hospitalization. This strategy helped optimize the burden on municipal hospitals and completely yielded good results. According to our estimates, less than 5% of patients with CT-0 and CT-1 to CT-2 were hospitalized as their condition worsened [10].

A chain of outpatient CT centers (OCTC) was established in municipal polyclinics to streamline the screening, routing, and real-time monitoring of patients with COVID-19. All 48 CT scanners in OCTCs were connected into a common digital network powered by ERIS EMIAS. This solution allowed radiologists to carry out distant reading of imaging results and therefore massively reduced the risk of getting infected, the importance of which can barely be overestimated.

During the pandemic, the activities of all Moscow Health Care Department screening programs have been suspended, so radiographers and surgical nurses were re-assigned to OCTCs. To prevent the spread of infection among patients and healthcare workers, the OCTC facilities were segregated into "red," "buffer," and "green" zones. The red zone contains scanning equipment, cleaned with disinfectants after each patient. All medical personnel assigned to

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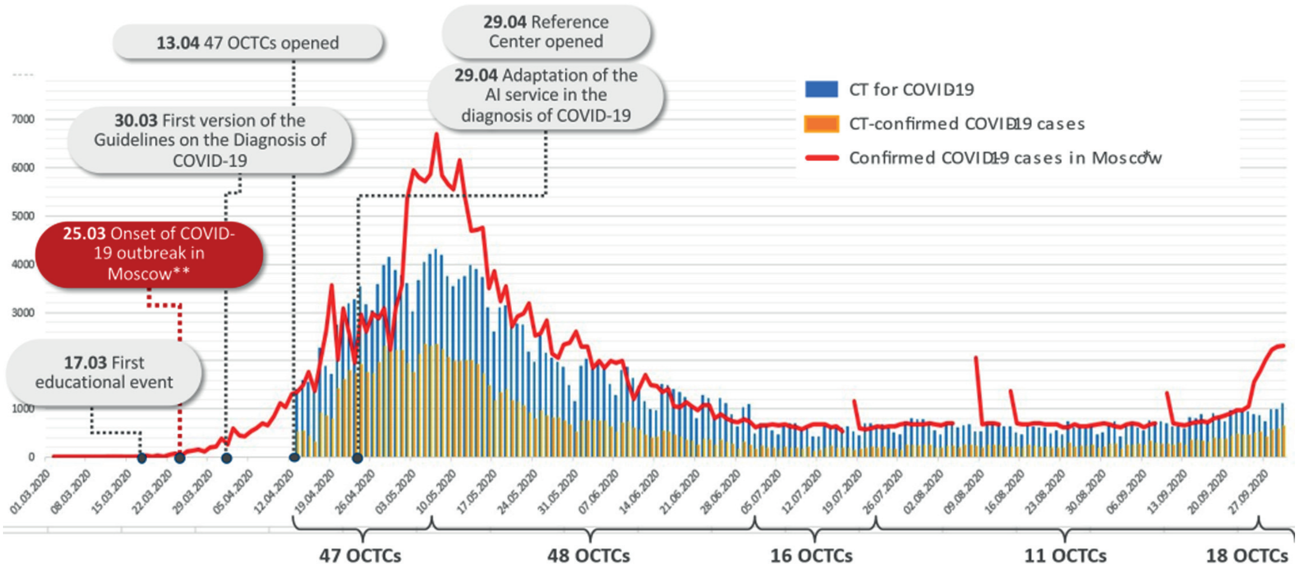

Fig. 1. Activation of the diagnostic radiology resources during the COVID-19 pandemic in Moscow.

the red zone were provided with grade 3 personal protective gear. In the buffer zone, the healthcare workers put on and take off their PPE; the zone is divided into three areas: used PPE area, disinfection area, and clean PPE area. Finally, the green zone contains doctors' offices and control area.

As part of measures taken to implement the strategy, health authorities established the Moscow Radiology Reference Center to supervise the quality of readings, provide distant consultations, and secure administrative and clinical support for OCTC workers.

Social media and messengers became an additional tool that brought together various specialists. An example is the "MRO.LIVE club for radiologists and radiographers" Telegram channel with 3,228 subscribers, most of which are medical imaging specialists. The channel became an invaluable tool for communication and real-time consultations. This is also a place where clinicians share information about the current status of the pandemic, regulatory documents, and educational activities.

The inflow of new health workers and rapid accumulation of scientific knowledge about the diagnosis of COVID-19 called for more educational programs for medical personnel. We have developed several short-term online courses and interactive webinars for different target audiences, such as OCTC administrators, radiologists, radiographers and assistants. Between February and October of 2020, our courses and webinars were attended by over 50,000 specialists. Approximately 10,500 radiographers specializing in different imaging modalities underwent training on chest CT.

To recognize COVID-19 signs, 149 imaging devices from 85 medical facilities in Moscow were connected to an artificial intelligence (AI) service. From April 29 to October 19, the AI service evaluated over 350,000 CT studies for COVID-19 signs. The AI system has accuracy and sensitivity of 0.91, specificity of 0.92, false-negative rate of 7.4 %, and false-positive rate of 1.6%. The implementation of the AI technology to OCTC allowed automation of information delivery, which helped clinicians prioritize the studies in their worklists. This experiment demonstrated the functional capabilities of the automated analysis of medical images by an algorithm that establishes the location of abnormalities and sends notifications to specialists, along with the practical value of the automated preparation of draft radiology reports. In addition, employees of the Moscow Center for Diagnostics & Telemedicine developed and opened free access to the world's largest reference dataset on COVID-19[5].

As of October 19, 2020, OCTC specialists have conducted 268,567 CT studies. The record was achieved by one CT scanner that made 204 CT studies in 1 day. Pneumonia signs were detected in 130,138 patients, 126,761 of which were diagnosed with "clinically confirmed COVID-19 case". As a result, over the specified period, 34.5% of all diagnoses in Moscow were established using medical imaging techniques.

Despite the 24/7 operation, the OCTC personnel were successfully shielded from the infection. In total, the workforce of 48 Moscow outpatient centers consisted of 485 radiologists and 775 radiographers. The average number of infected radiologists was 10 ± 4 (2.1%); the number of affected radiographers exceeded that for a small margin at 22 ± 12 (2.8%).

[5] Dataset MosMedData: COVID-19_1110. Available at: https://mosmed.ai/datasets/covid19_1110. Accessed: October 16, 2020.

The developed operation strategy of Moscow's radiology service (Fig. 1) secured even distribution of health care burden during the pandemic and minimized losses among the medical personnel. Clinical experts played an important role in holding down the infection levels with the help of widely available, well-timed, and high-quality diagnostic and routing services. Emergency activation of the primary care segment and accessible radiology scanning solutions secured sustainable detection of disease symptoms, streamlined the delivery of diagnostic data, and ultimately helped reach the plateau on disease statistics. At present, the world is facing a second wave of the pandemic, and the Moscow Health Care Department is willing to stay ahead of the game at all times. Considering the massive uptake of laboratory testing, the need for mass screening with medical imaging is not as urgent anymore. With that said, our developments and accumulated expertise are among the top requested in other regions of the Russian Federation and abroad. We continuously share our knowledge through educational programs, webinars, and academic publications.

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Диагностическая ценность ультразвукового исследования лёгких для выявления COVID-19: систематический обзор и метаанализ

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Обоснование. При оценке степени тяжести состояния пациентов с COVID-19 опираются в первую очередь на объём поражения лёгочной ткани. Существует ряд диагностических подходов, позволяющих анализировать этот показатель, каждый из которых сопряжён с определёнными ограничениями. Цель и дизайн исследования, характеристики наблюдаемых пациентов, доступность оборудования — все эти параметры способны повлиять на выбор оптимальной методики.

Цель — провести оценку чувствительности и специфичности ультразвукового исследования (УЗИ) в качестве метода анализа степени поражения лёгких у пациентов с COVID-19 посредством систематического обзора статей на английском языке, доступных в базах данных PubMed и Google Scholar. Ключевые слова для поиска: lung ultrasound, chest ultrasound, thoracic ultrasound, ultrasonography, COVID-19, SARS-CoV-2, coronavirus, diagnosis, diagnostic value, specificity и sensitivity. В обзор включали только исследования, затрагивавшие вопросы диагностической точности УЗИ лёгких для пациентов с подозрением на COVID-19. В качестве эталонных методов рассматривали компьютерную томографию грудной клетки, детекцию вирусной РНК с помощью полимеразной цепной реакции с обратной транскрипцией или лабораторные данные. Извлечение статей проводили два автора независимо друг от друга с заполнением заданных полей стандартизованной таблицы и последующей оценкой индикаторов качества исследования. Для анализа и группировки данных о чувствительности и специфичности УЗИ лёгких для оценки объёма изменённой лёгочной ткани в отобранных работах использовали модель случайных эффектов. По заданным критериям включения подходили 16 работ, однако только в трёх проводили разделение пациентов на чётко заданные группы по тяжести заболевания. Из остальных работ для оценки вторичных результатов использовали значения чувствительности и специфичности УЗИ лёгких для диагностики COVID-19 вне зависимости от состояния пациента. Наблюдаемая гетерогенность для первичных и вторичных результатов сохранялась при группировке исследований по сценариям (скрининг, оценка тяжести заболевания) и когортам пациентов. УЗИ лёгких показало наиболее высокую точность для подтверждения поражения лёгких у пациентов с диагностированной тяжёлой коронавирусной инфекцией COVID-19 (чувствительность 87,6 ± 12,3%, специфичность 80,5 ± 7,1%). При этом самую низкую точность метод продемонстрировал у пациентов с заболеванием лёгкой степени тяжести (чувствительность 72,8 ± 7,1%, специфичность 74,3 ± 2,7%).

Заключение. УЗИ лёгких может быть использовано у пациентов с подтверждённым COVID-19 для выявления значительных повреждений лёгочной ткани. Диагностическая ценность метода для оценки умеренных и незначительных поражений лёгких относительно низкая.

Ключевые слова: COVID-19; УЗИ лёгких; оценка доли поражения; диагностическая ценность; чувствительность; специфичность.

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Diagnostic value of lung ultrasound in COVID-19: systematic review and meta-analysis

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BACKGROUND: Effective and safe tools assisting triage decisions for COVID-19 patients could optimize the pressure on the healthcare system. COVID-19 often has respiratory manifestations, and medical imaging techniques provide an opportunity to assess the disease's severity.
AIMS: To estimate the sensitivity and specificity of lung ultrasound for different degrees of pulmonary involvement in COVID-19 patients by a systematic review of English articles using PubMed and Google Scholar databases. Search terms included lung ultrasound, chest ultrasound, thoracic ultrasound, ultrasonography, COVID-19, SARS-CoV-2, coronavirus, diagnosis, diagnostic value, specificity, and sensitivity. Only studies addressing lung ultrasound diagnostic accuracy for patients with suspected COVID-19 using thoracic computed tomography, reverse transcription polymerase chain reaction, or laboratory data as a reference standard were included. Independent extraction of articles was performed by two authors using predefined data fields with subsequent assessment of study quality indicators. The random-effect model was used to analyze and pool lung ultrasound sensitivity and specificity across the included studies. Sixteen studies met our inclusion criteria, but only three of them divided patients into distinct and defined groups depending on the disease severity. We used the remaining studies' data to assess the secondary outcomes: the values of sensitivity and specificity of lung ultrasound for COVID-19 regardless of the patient's clinical status. Heterogeneity for primary and secondary outcomes was observed that remained when pooling for different scenarios (screening, assessing severity) and cohorts of participants. Lung ultrasound had the highest accuracy for confirmed COVID-19 patients with severe disease (sensitivity 87.6% ± 12.3%, specificity 80.5% ± 7.1%), and the lowest accuracy for the patients with mild disease (sensitivity 72.8% ± 7.1%, specificity 74.3% ± 2.7%).
CONCLUSIONS: Lung ultrasound can be used in patients with confirmed COVID-19 to detect serious damage to the lung tissue. The diagnostic value of the method for assessing mild and moderate lung lesions is relatively low.

Keywords: COVID-19; lung ultrasound; severity grade estimate; diagnostic value; sensitivity; specificity.

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肺部超声检测COVID-19的诊断价值：系统综述和荟萃分析

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论证：在评估COVID-19患者病情的严重程度时，主要依赖肺组织损伤的体积。有许多诊断方法允许分析该指标，每一种方法都有一定的局限性。研究的目的和设计，观察患者的特点，设备的可用性，所有这些参数都可以影响最佳方法的选择。
目的是通过对PubMed和Google Scholar数据库中相关英文文章的系统回顾，评估超声作为一种分析COVID-19患者肺损伤程度的方法的敏感性和特异性。关键词：lung ultrasound; chest ultrasound; thoracic ultrasound; ultrasonography; COVID-19; SARS-CoV-2; coronavirus; diagnosis; diagnostic value; specificity; sensitivity该综述仅包括了针对疑似COVID-19患者肺部超声诊断准确性问题的研究。参考方法包括胸部CT、逆转录聚合酶链反应检测病毒RNA、实验室数据等。论文由两位作者独立抽取，填写标准化表格的指定字段，然后对研究质量指标进行评价。为了分析和分组所选研究中肺超声评估肺组织改变体积的敏感性和特异性的数据，使用了随机效应模型。根据规定的纳入标准，适合16项研究，但仅对3例患者根据疾病严重程度划分明确组。通过其他有关材料，为了评估次要结果，使用了肺部超声诊断COVID-19的敏感性和特异性值，而不考虑患者的病情。当研究根据筛查、疾病严重程度评估和患者队列进行分组时，观察到的主要结果和次要结果的异质性得以保持。肺部超声诊断重症冠状病毒感染COVID-19患者肺损害的准确性最高（敏感性为87.6±12.3%，特异性为80.5±7.1%）。同时，该方法在轻度疾病患者中的准确率最低（敏感性为72.8±7.1%，特异性为74.3±2.7%）。
结果。肺部超声检查可用于确诊COVID-19的患者，以检测肺组织的严重损害。该方法评估轻微-中度肺损伤的诊断价值相对较低。

关键词：COVID-19；肺部超声；病变部位评估；诊断价值；敏感性；特异性

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ABBREVIATIONS

CI — confidence interval
SMD — standard mean difference
CT — computed tomography
US — ultrasound
RT-PCR — reverse transcription polymerase chain reaction
ICD — International Classification of Diseases

INTRODUCTION

As of September 16, 2020, there are 29,155,581 confirmed cases globally, with 926,544 deaths [1] from the COVID-19 pandemic. The impact of the end of the summer vacation period and schools re-opening on the epidemic is uncertain. However, there is a possibility of a second wave of the disease [2], if it will follow a high transmission scenario. Amid rising number of new cases, Israel was the first developed country to announce a second nationwide lockdown [3]. Presently, since June 30, 2020, more than 700 cases of SARS-CoV-2 infection have been detected in Moscow. Effective and safe patient triage tools could aid decrease the COVID-19-associated pressure on the healthcare system. Several laboratory parameters help assess the disease severity, such as calculation of the viral load [4], platelet count [5], D-dimer concentrations [6], and others [7]. COVID-19 often leads to respiratory manifestations, and therefore medical imaging is one of the main techniques to assess its severity in patients [8]. Among the imaging modalities, including radiography, computed tomography (CT), and ultrasound (US), CT offers great sensitivity in detecting COVID-19-related findings [9]. Because of this, some experts suggest making it a diagnostic standard. CT imaging was one of the main diagnostic and triage tools in Moscow, Russia, during the lockdown period [10]. Unfortunately, CT it is not widely available and is associated with potential harm from exposure to ionizing radiation. Lung US could compensate for that, being a widespread and safe method. The technique is appealing, especially for pregnant women, children, and critically ill patients. Recent systematic reviews explore the potential utility of lung US [11, 12]. However, there are not enough scientific data to establish the functionality of this approach in making clinical decisions depending on the severity of the disease [13].

We reviewed currently available studies addressing cohorts of COVID-19 patients for the disease severity using US compared to CT, RT-PCR, and laboratory data, in order to assess the sensitivity and specificity of lung US for different degrees of pulmonary involvement.

METHODS

This manuscript follows the PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions [14].

Eligibility criteria

Types of studies. Inclusion criteria: (i) any study evaluating the performance of lung US in diagnosing COVID-19; (ii) studies reporting US sensitivity and specificity values or providing enough information to construct a 2 × 2 confusion matrix; and (iii) we placed no restrictions regarding country, patient age, sex, and race. Exclusion criteria were as follows: (i) studies with unavailable full texts; (ii) studies on non-human subjects; (iii) case reports, case series, and systematic review studies; and (iv) studies published before January 1, 2020.

Types of participants. Hospital patients of any age with signs and symptoms of COVID-19-associated pneumonia confirmed by CT, RT-PCR, or serological tests (ICD codes U07.1, U07.2).

Types of intervention. Studies comparing the diagnostic value of lung US, including point-of-care US (POTUS) with chest CT, chest radiography, and clinical follow-up data.

Types of outcome measures. Primary outcome measures: numerical values of sensitivity and specificity of lung US in COVID-19 patients of different severity grades. Secondary outcome measures: numerical values of sensitivity and specificity of lung US and POTUS for COVID-19 patients regardless of the disease severity.

Information sources. Studies were identified by searching the electronic databases PubMed and Google Scholar. The last search was run on September 1, 2020.

Search. We performed two types of searches in the PubMed database, using MeSH terms and text keywords since it takes about a month for PubMed to assign a MeSH term for a published study:

1) (“Coronavirus infections/diagnosis”[MeSH] OR “Coronavirus infections/diagnostic imaging”[MeSH]) AND “Ultrasonography”[MeSH]
2) (“lung ultrasound” OR “chest ultrasound” OR “thoracic ultrasound” OR “ultrasonography”) AND (COVID-19 OR “SARS-CoV-2” OR “coronavirus”) AND diagnosis

We used the query string “lung ultrasound diagnostic value specificity sensitivity COVID-19” to search the Google Scholar database.

Study selection. Two reviewers (RVR and DVL) assessed for eligibility in a standardized manner by an automatic search for words “sensitivity” and “specificity” in full texts. Three other researchers (NNV, NSK, and OAM) evaluated the selected manuscripts according to the study protocol to resolve discrepancies.

Data collection process and data items. We developed a data extraction sheet using the Google Spreadsheet service to ensure that all the reviewers have simultaneous and unrestricted access to the document. The data extraction sheet was pilot-tested on three randomly selected included studies and refined accordingly. Two reviewers (RVR and DVL) extracted the following data from the included studies: Authors, Affiliation, Title, Journal (or preprint service), Acceptance date, DOI, Population (number, age, % female, inclusion & exclusion criteria, medical centers location, start and end dates of the study), US protocol, US scoring, comparison protocol, comparison scoring, US outcome, and comparison outcome. The three other researchers (NNV, NSK, and OAM) verified the extracted data. Disagreements were resolved through a discussion among the authors. After the review started, we added the data from systematic reviews on specificity and sensitivity of reference standard methods if the values were not estimated in the included studies.

Risk of bias in individual studies. To assess the methodological issues associated with diagnostic accuracy studies, we followed the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) framework [15] recommended for systematic reviews by the Agency for Healthcare Research and Quality, Cochrane Collaboration. Four domains were used to organize each included study: patient selection, index test, reference test, and patient flow. A detailed description of each domain and judgment criteria are described in the Cochrane Handbook [16].

Statistical analysis. We used the random-effect model to analyze and pool lung US sensitivity and specificity across the included studies. To measure between-studies heterogeneity, we used estimates of τ^2, the percentage of variability I^2, and Cochran's Q-statistic. As a threshold we used I^2 values of 25% (low heterogeneity), 50% (moderate heterogeneity), and 75% (substantial heterogeneity) and p-values < 0.05. The meta-analysis was performed using the *dmetar* [17] package for R 3.6.3 [18].

RESULTS

Study selection. We included 16 studies in this review. The search in PubMed and Google Scholar databases provided 245 studies imported into a Mendeley library. Of these, six studies were discarded because they were conducted on non-human subjects. After adjusting for duplicates, 236 studies remained. Of these, 220 studies did not meet the criteria and were discarded after abstract or full-text reviewing (Figure 1). We examined the full texts of the remaining 16 studies [19–34], and only six of these analyzed the diagnostic accuracy of US in the context of the disease severity [19, 20, 27–30]. However, only three studies enrolled patients of all clinical grades: mild, moderate, and severe stages of the disease [19, 20, 28]. The other three studies included only critically ill patients [27, 29] or evaluated the prognostic value of lung US in predicting the need for non-invasive respiratory support [30]. A study by Veronese et al. stood out because they analyzed the data of bedridden nursing home patients, aged 84.1 ± 9.8 years [24]. For these patients, mortality was associated with a lung US score of 4 (maximum value 36), primarily due to this cohort's general health.

With the exception of the study by Hatamabadi et al. that provided only the seven-day results [34], the average follow-up period in the included studies was 34 ± 15 days. The included studies involved 1696 participants, of which 1121 had confirmed COVID-19. There were 13 single-center and three multicentric studies, two of which were conducted in France and one in China. In total, four studies were conducted in France, three in China, two studies each in the USA, Turkey, and Spain, and the remaining three came from Iran, Italy, and Israel (Figure 2). The mean or median age of participants ranged from 27 to 69 years (with the exclusion of the study of Veronese et al. [24]).

All studies had a test group (patients with confirmed COVID-19), while only five studies included a control group of SARS-CoV-2-negative participants [22, 25, 26, 31, 33]. Patients in the test group were diagnosed using the RT-PCR test. The specificity and sensitivity of lung US were estimated using RT-PCR in six studies [22, 24–26, 31, 33], clinical and laboratory data in two studies [28, 29], and chest CT in seven studies [19, 20, 23, 27, 30, 32, 34] as a reference standard.

Risk of bias. The main sources of bias came from the patient selection domain (Figure 3). The majority of studies (75%) included previously diagnosed patients. However, in all the studies, the participants met the criteria of the review protocol. The specialists performing lung US and analyzing the results were not blinded to the diagnosis, which could also be a potential source of bias.

Seven studies properly reported the details of both index and reference standard tests. The interobserver variability was estimated only in three studies [21, 25, 32]. Three studies only (19%) reported the interval between the two tests, but the majority (87%) correctly indicated whether all patients used the same reference standard.

Scoring systems. The included studies used different scoring systems to assess the presence and severity of the disease. Dividing the imaging zone into separate regions, and providing a score reflecting the degree of pul-

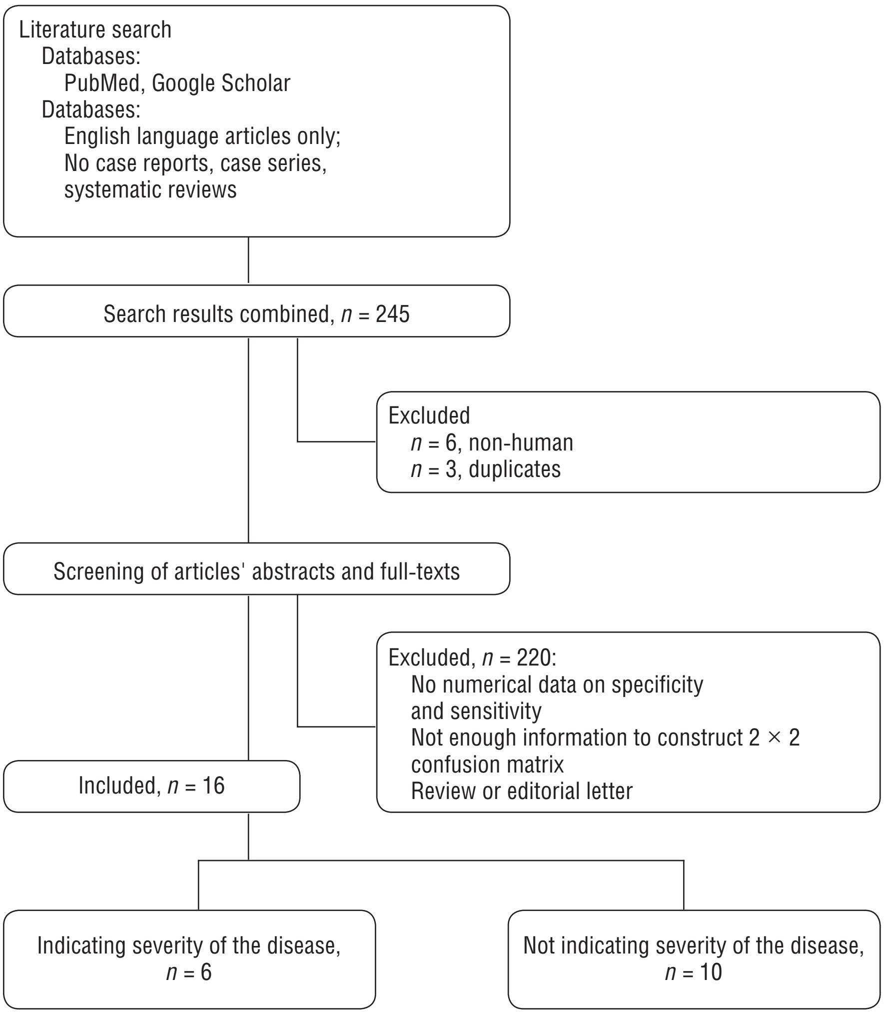

Figure 1. Flow diagram of the study selection.

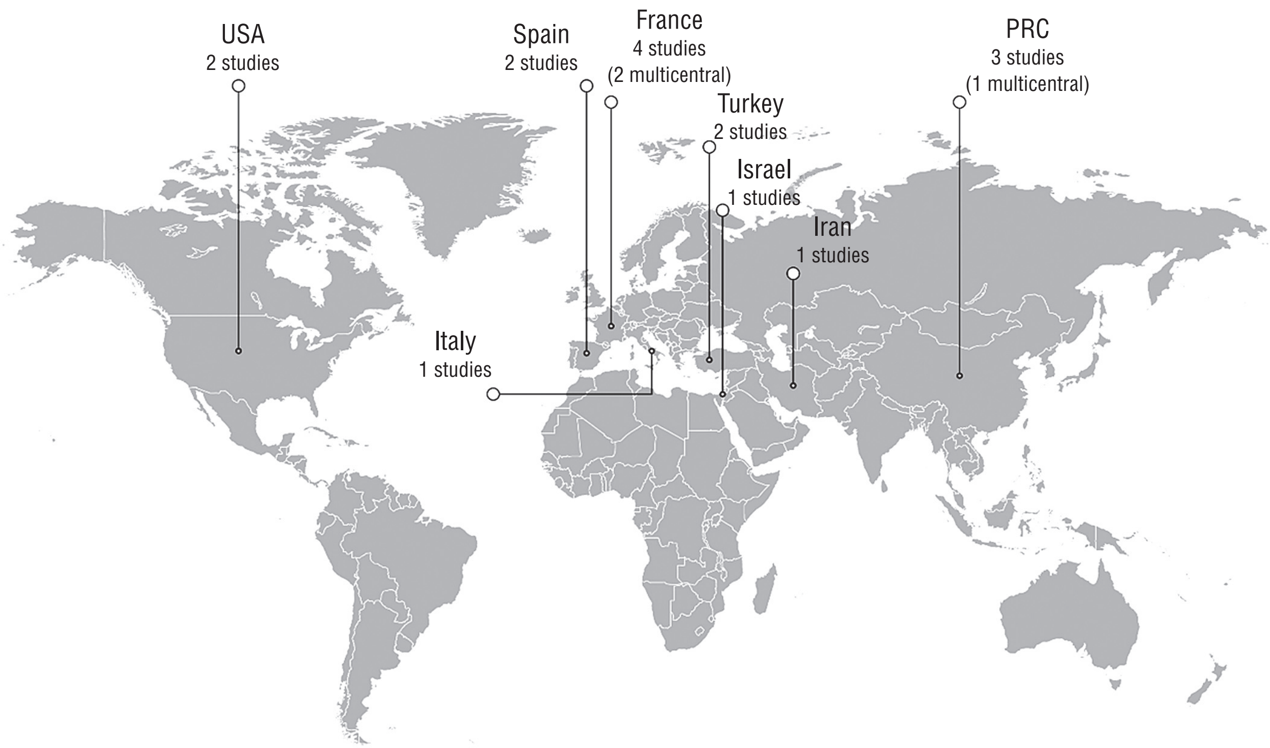

Figure 2. The map of studies included in the review.
Note: the map template had been purchased from Shutterstock [35].

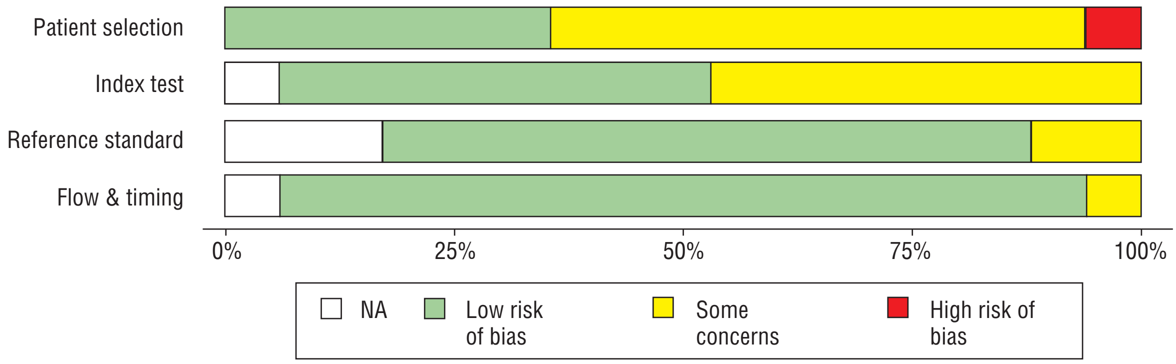

Figure 3. Bar chart of risk of bias for the 16 included studies.

monary involvement to each region was common to most systems (87%). The total lung US score was calculated as the sum of individual scores. The most popular scoring system divided each hemithorax into six regions, with each region scored on a scale from 0 to 3, and a total score ranging from 0 to 36 [19, 20, 23, 24, 28, 30]. Three studies collected the lung US results from eight zones [27, 32, 33] but used a different scoring approach. While two groups scored each zone on a scale from 0 to 3 (total value 0–24) [27, 32], Favot et al. analyzed the lung US images for the presence of different patterns [33]. Two studies divided the chest wall into ten zones but used different severity scales with a maximum value of 40 [29] or 10 [34]. Yassa et al. collected the scores in a range from 0 to 3 from 14 zones (total value 0–42) [25, 26]. Finally, two groups performed a qualitative assessment of the lung involvement based on the US findings [21, 22].

Diagnostic accuracy of lung US. All included studies reported the lung US sensitivity and specificity values, with sensitivity ranging from 15.6% to 100% and specificity ranging from 51.9% to 100%. However, only three studies estimated the diagnostic performance of a reference standard test [23, 27, 32]. For the estimating of values in the review, we used the meta-analysis data on the sensitivity and specificity of RT-PCR [35] and chest CT [36]. For the studies using clinical and laboratory data as a reference standard test [28, 29], the control specificity and sensitivity values were set at 100% (Figure 3).

According to the meta-analysis results, lung US has a specificity 81.6% ± 13.3% and sensitivity 79.4% ± 21.4% in diagnosing COVID-19. However, the Cochran's test revealed a significant heterogeneity of the data: Q = 2244.8, $p < 0.001$, and Q = 1127.7, $p < 0.001$, for sensitivity and specificity, correspondingly.

The observed heterogeneity could be associated with the fact that the included studies assessed the diagnostic value of lung US for different purposes and cohorts of participants. For further analysis, we excluded the study by Veronese et al.[24]. We divided the remaining studies into two groups: in the first group, the researchers used US to screen for COVID-19 [19, 21–23, 25, 26, 31, 32], in the second, they used US to evaluate and follow-up critically ill patients [19, 27, 30, 32, 33]. We also did not include the studies by Lichter et al. [28] and Zhao et al. [29] in the second group, because the authors estimated the prognostic value of lung US to predict mortality and refractory situation, correspondingly. Lichter et al. reported a 62% sensitivity and 74% specificity in the ROC analysis of 30-day mortality, the cut-off value for lung US score was 18 (maximum value 32) [28]. According to Zhao et al., using the lung US score cut-off value of 32 points (maximum value 40) predicted a refractory situation with a 57% sensitivity and 89% specificity [29].

The index test characteristics remained heterogeneous, with the lowest Q-statistic and variability percentage obtained for lung US sensitivity in critically ill patients (Table 1).

Table 1. Lung US efficiency for patients with COVID-19

Group	Sensitivity		Q	I^2, %	Specificity		Q	I^2, %
	Mean, %	SD, %			Mean, %	SD, %		
Screening	79,6	21,6	694,2	99,0	79,5	16,1	345,0	98,0
Severe	87,6	12,3	158,9	97,5	80,5	7,1	379,6	98,9
Moderate	72,8	7,1	11,24	91,1	74,3	2,7	0,26	0,0
Mild	80,4	16,5	59,5	98,3	66,6	27,0	33,3	97,0

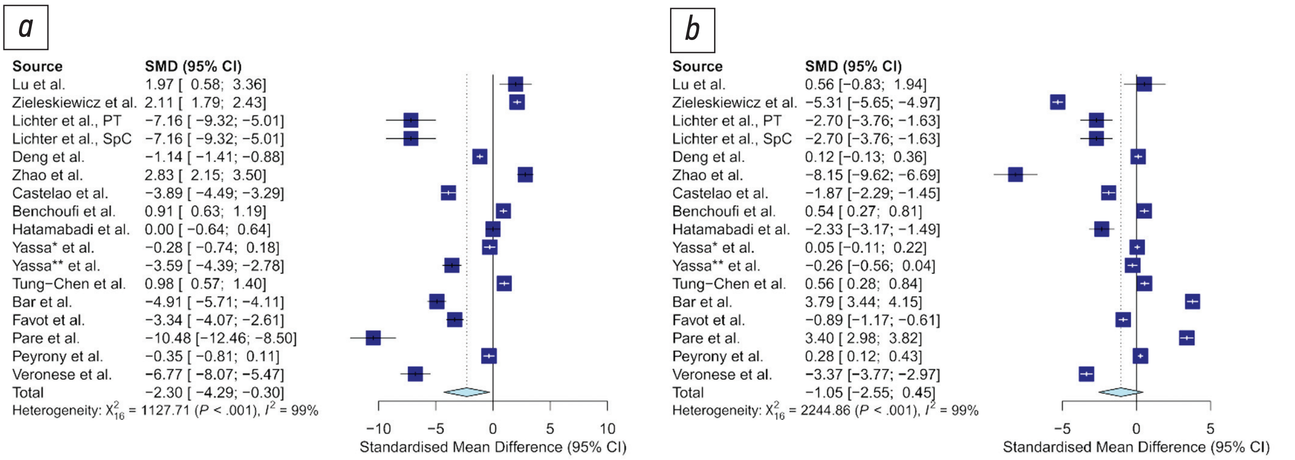

Figure 4. Forest plots of pooled specificity (A) and sensitivity (B). The symbols * and ** denote studies by Yassa et al. on interobserver agreement [25] and the role of lung US in COVID-19 screening [26], correspondingly.

We also pooled the sensitivity and specificity values for patients with different degrees of pulmonary involvement. From the data provided in the study by Lichter et al.[28], it was not possible to extract the numerical data to estimate the characteristics. Therefore, we did not include this study into the meta-analysis. In the study by Zieleskewicz et al., we obtained the sensitivity and specificity values with the maximum Youden index from the three zones on the ROC curve according to the lung US score thresholds [20].

The data was heterogeneous, except for the lung US specificity in moderately ill patients (Table 1). Note that we used the results for moderately and mildly ill participants from only two studies in this meta-analysis, and both of them did not include a control group of patients.

DISCUSSION

The variety of scoring systems in the included studies makes it impossible to directly compare the lung US score cut-off values used to estimate the outcomes. However, regardless of the scoring system, almost all authors agree that patients with severe disease had higher lung US score values than patients with moderate and mild disease. The first exception to this was the study by Veronese et al., where the authors did not find a significant difference in mortality risk between nursing home patients with a lung US score ≥ 4 and < 4 (maximum value 32) [24]. The authors did not interpret this observation, but we believe it is related to the general health of the nursing home residents, which were older adults, suffering from dementia, and bedridden. The other exception was the study by Benchoufi et al., which showed that the performance of the lung US scoring system used by the authors was lower to predict the disease classified as severe by chest CT compared with *normal* vs. *pathologic* and *normal or mild* vs. *moderate or severe* [32].

Overall, in confirmed symptomatic COVID-19 patients with severe disease, the lung US and CT scores positively correlated. According to our meta-analysis, lung US has a sensitivity of 88% and 80% specificity in this group (see Table 1). That is a specific cohort of patients, but for them, lung US has significant advantages compared with chest CT in terms of health risks and logistical limitations.

Low lung US scores were also valuable to exclude severe COVID-19-associated pneumonia. According to Zieleskewicz et al., chest CT would not be required if the initial US examination had a score <13 (out of 36) [20]. Lichter et al. reported that lung US could predict good clinical outcomes for symptomatic patients without any pleural thickening or subpleural consolidations [28]. Despite the relatively low efficiency of lung US in assessing mild lung lesions [19], this feature could have practical value for symptomatic patients in making triage decisions.

The highest discrepancy between the lung US and chest CT scores was observed for moderately ill patients. For this group of patients, lung US was least sensitive (see Table 1). Zieleskewicz et al., in their study, called the zone on the ROC curve from which we obtained the data, “a grey zone with inconclusive values” [20]. Therefore, despite the relatively modest statistical heterogeneity, the diagnostic value of lung US for moderate lung lesions is relatively low.

Screening for COVID-19 using lung US findings has several advantages in pregnant women. In the study of Yassa et al., 17% of the pregnant women, who had undergone a lung US exam and were RT-PCR-positive, initially had negative RT-PCR results. The RT-PCR test was repeated after a week due to their abnormal US findings [26]. Note that the specificity of lung US according to our meta-analysis, was significantly higher than the specificity of chest CT, a “gold standard” for medical imaging: 79% vs. 31%, correspondingly. It might be associated with the fact that most included studies were conducted in conditions of high pre-test probability. There was an evident patient selection and index test risk of bias that could affect the observed specificity value (see Figure 3).

Chest CT is superior to lung US in differential diagnostics of lung pathologies since it is sensitive for alternative diagnoses [37, 38]. Contrary to that, lung US cannot distinguish between pulmonary alterations: pneumonia, lung cancer, or atelectasis, which may show the same echographic pattern [11, 39]. Moreover, the accuracy of the lung US exam is highly dependent on the operator's expertise level and could be affected by a pre-test probability of the disease. For example, in the study by Tung-Chen et al., three patients had lung US findings compatible with COVID-19; two patients were eventually diagnosed with viral bronchiolitis, and the other patient had metastatic pulmonary disease. The inter-rater agreement in the included studies, when reported, could be as low as 68%, which significantly reduces the applicability of the technique. However, a quick bedside lung US exam proved useful for real-time evaluation and monitoring of patients with rapidly progressing disease [19, 28].

Our study has limitations. Conventionally, at least five studies should be used for a meta-analysis. Although our final library contained 16 studies, the data was incomplete. For some analyses, we used the highly heterogeneous values obtained from only two studies. Significant data heterogeneity is also associated with the differing patient population, index test and reference standard protocols, and the outcome definitions across the included studies.

CONCLUSIONS

In 2020, several meta-analyses on lung US applicability for COVID-19 patients were published. All agree that the presence of lung US findings, although nonspecific, could be used for diagnosis, triage, and follow-up of the subjects with SARS-CoV-2 infection. Unfortunately, none of them focused on distinguishing between patients with different clinical status and prognosis. Chest CT is the gold standard in assessing the severity of the disease. However, depending on the patient cohort and the disease stage, other techniques could be advantageous. Lung US has adequate sensitivity and specificity for confirmed COVID-19 patients with severe lung involvement that have a risk of adverse events associated with transfer and exposure to ionizing radiation. Lung US is preferable for critically ill patients, pregnant women, children, and bedridden aged population. The technique is applicable for triage of patients with mild symptoms to rule out lung tissue damage. In patients with moderate disease, the diagnostic value of lung US is the lowest.

The high heterogeneity of the sensitivity and specificity values should be addressed in further studies. We believe that these studies need to be performed on large randomized cohorts of patients following a systematic protocol with clear and standardized definitions of the disease stages and including a control group of participants. Another issue that requires future research is the sensitivity and specificity of different scoring systems used to assess the severity of the disease.

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All authors made a significant contribution to the search and analysis work and preparation of the article, read and approved the final version before publication.

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Прогнозирование исходов при лабораторно верифицированном COVID-19 по данным компьютерной томографии органов грудной клетки: ретроспективный анализ 38 051 пациента

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Обоснование. В условиях сложившейся эпидемиологической ситуации компьютерная томография органов грудной клетки (КТ ОГК) играет важную роль в диагностике заболевания. Клинические и КТ-данные позволяют врачам в короткие сроки установить вероятность наличия и прогноз у пациентов с COVID-19.

Цель — прогнозирование исходов у лабораторно верифицированных больных COVID-19 по данным КТ ОГК с помощью полуколичественной визуальной шкалы степени поражения лёгочной паренхимы (шкала КТ0–КТ4).

Материал и методы. Выполнен ретроспективный анализ выгрузки историй болезни из Единого медицинского информационного-аналитического сервиса (ЕМИАС) и протоколов из Единого радиологического информационного сервиса (ЕРИС) в период с 01.03.2020 по 30.07.2020. В исследование включены истории болезней пациентов с диагнозом U07.1 по МКБ-10 (лабораторно верифицированная коронавирусная инфекция), которым с 1 марта по 30 июля 2020 г. включительно проведена КТ ОГК по направлению врача-терапевта при подозрении на внебольничную пневмонию, вызванную COVID-19; максимально допустимый срок между лабораторной верификацией и КТ ОГК — не более 5 дней. Срок наблюдения за каждым пациентом — не менее 30 сут от даты проведения КТ. Исследования были выполнены в 48 медицинских организациях, оказывающих первичную медицинскую помощь взрослому населению Москвы. Не вошли в исследование пациенты, у которых результаты теста полимеразной цепной реакции на COVID-19 были отрицательными к 30.07.2020. Шкала КТ0–КТ4 рекомендована к применению в Российской Федерации для оценки объёма поражения паренхимы лёгкого при подозрении на COVID-19.

Результаты. Итоговый объём выборки — 38 051 пациент. По результатам исследования выявлено, что для категории КТ4 риск смерти выше в 3 раза по сравнению с категорией КТ0. По кривым Каплана–Мейера для анализа выживаемости доля выживших пациентов в категории КТ3 почти в 3 раза ниже (HR = 2,94), чем в категориях КТ0–КТ2. Кроме того, установлено, что чем выше исходная категория КТ, тем ниже риск ухудшения. Время до госпитализации снижалось при увеличении категории по данным КТ ОГК.

Заключение. Визуальная шкала КТ0–КТ4 может быть использована в качестве предиктора исходов (госпитализаций и летальных исходов) у пациентов, которым при подозрении на COVID-19 выполнена КТ ОГК на базе первичного звена здравоохранения.

Ключевые слова: COVID-19; внебольничная пневмония; компьютерная томография.

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Chest computed tomography for outcome prediction in laboratory-confirmed COVID-19: A retrospective analysis of 38,051 cases

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BACKGROUND: In the current epidemiological situation, computed tomography (CT) of chest organs plays an important role in disease diagnosis. Clinical and CT data allow physicians to quickly establish the probability of the presence and prognosis of patients with coronavirus disease 2019 (COVID-19).
AIMS: This study aimed to predict outcomes in patients with laboratory-confirmed COVID-19 based on chest CT and a semi-quantitative visual pulmonary lesion grading system (CT 0–4).
MATERIALS AND METHODS: A retrospective analysis of the Unified Medical Information and Analytical Service and Unified Radiological Information Service records from March 01, 2020 to July 30, 2020 was performed. The inclusion criteria were as follows: patients diagnosed with U07.1 (laboratory-verified coronavirus infection) from March 01, 2020 to July 30, 2020 and referred for a chest CT by a physician with suspected community-acquired pneumonia caused by COVID-19; the maximum period between laboratory verification and CT was not more than five days. The observation period for each patient was at least till 30 days from the date of CT. CT was performed in 48 medical organizations providing primary medical care to adults in Moscow. The exclusion criterion was a negative reverse transcription-polymerase chain reaction results by July 30, 2020. The CT 0–4 scale is recommended for use in the Russian Federation to estimate the volume of lung parenchyma lesions when COVID-19 is suspected.
RESULTS: The total sample volume was 38,051 patients. In this study, the risk of death was three times higher for CT-4 than for CT-0. In the Kaplan–Meier survival curve, the survival rate of patients in the CT-3 category was almost three times lower (hazard ratio = 2.94) than in the CT 0–2 categories; in addition, the higher the initial category of CT, the lower the risk of deterioration. The time for hospitalization decreased with the increase in the CT grade.
CONCLUSION: The visual CT 0–4 scale can be used to predict outcomes, such as hospitalizations and deaths, in patients suspected of COVID-19 who underwent chest CT in primary health care.

Keywords: COVID-19; community-acquired pneumonia; computed tomography.

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基于胸部CT的实验室验证**COVID-19**预后预测：**38,051**例患者的回顾性分析

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论证：在目前的流行病学情况下，胸部器官CT（胸部器官的计算机断层扫描）在该病的诊断中起着重要的作用。临床和CT数据使医生能够快速判断COVID-19患者的存在概率和预后。

目的：预测实验室证实的COVID-19患者的结果，基于胸部器官CT，使用肺实质损伤程度半定量视觉量表（CT0—CT4量表）。

材料与方法。对2020年3月1日至2020年7月30日期间从统一医疗信息和分析服务处（UMIAS）和从统一放射信息服务处（ERIS）卸载的医疗记录和协议进行了回顾性分析。本研究纳入了根据ICD-10诊断为U07.1患者的病历（实验室确诊新型冠状病毒感染病例）。从2020年3月1日至7月30日，这些患者在疑似COVID-19引起的社区获得性肺炎的内科医生的指导下接受胸部器官CT检查；实验室检查和胸部器官计算机断层扫描之间最长允许的时间不超过5天。每位病人的随访期由CT日期起计最少为30天。这项研究是在向莫斯科成年人口提供初级医疗保健的48个医疗机构中进行的。本研究不包括截至2020年7月30日COVID-19聚合酶链反应试验结果为阴性的患者。CT0-CT4量表推荐在俄罗斯联邦用于评估疑似COVID-19病例肺实质损害的程度。

结果。样本量为38,051例。根据研究结果，CT-4类患者的死亡风险比CT-0类患者高3倍。Kaplan-Meyer 生存曲线显示，CT-3类患者的存活比例比CT0-CT2类患者低3倍（HR = 2.94）。此外，发现了CT的初始类别越高，恶化的风险越低。根据胸部器官CT显示，住院时间随类别的增加而减少。

结果。CT0-CT4的视觉尺度可用于预测疑似COVID-19患者的预后（住院和死亡），如果患者在初级卫生保健的基础上接受了胸部器官CT检查。

关键词：COVID-19；社区获得性肺炎；计算机断层扫描

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INTRODUCTION

On March 11, 2020, the World Health Organization declared COVID-19 caused by the SARS-CoV-2 virus a pandemic [1]. According to official data, by the third quarter of 2020, there were more than 29 million confirmed cases and more than 940 thousand deaths worldwide [2].

Given the current epidemiological situation, chest computed tomography (CT) plays an essential role in diagnosing the disease. Clinical and CT data allow doctors to establish the probability and prognosis in patients with COVID-19 within a short time [3]. It should be noted that there are no specific signs of COVID-19 in chest CT, but bilateral peripheral ground-glass opacities are most often visualized, with a predominantly basal involvement [4,5]. Besides, quantitative chest CT analysis allows for COVID-19 patient triage [6]. Thus, Colombi et al. presented a quantitative assessment of pulmonary parenchyma lesions using an open-source software and established a high correlation between preserved, well-ventilated pulmonary tissue and outcomes (transfer to the intensive care unit or death) [7]. The extent of pulmonary lesions in COVID-19 can be fully and automatically assessed using machine learning algorithms [8].

Due to the epidemiological situation, it is necessary to create and critically evaluate prognostic models based on clinical data [9]. In the Russian Federation, due to the large patient flow, an "empirical" visual scale is recommended for the rapid and standardized assessment of lung lesions detected by chest CT [10].

This study aimed to predict the outcomes of laboratory-confirmed COVID-19 patients from their chest CT data using a semi-quantitative visual scale for grading pulmonary lesions.

MATERIALS AND METHODS

The Independent Ethical Committee of the Moscow Regional Branch of the Russian Society of Radiologists approved this retrospective study. Informed consent was not required due to the retrospective design of the study (absence of the prospective part of the study intervening in the treatment or diagnosis). A total of 240985 patients were selected from UMIRAS and Unified Radiological Information Service (URIS). We excluded 202934 patients due to lack of laboratory confirmation or data on the CT0–4 scale.

Patients

The analysis of the Unified Medical Information and Analytical Service (UMIAS) and URIS protocols for the period from 01/03/2020 to 30/07/2020 inclusive was performed. The study included patients according to the following criteria: patients diagnosed with U07.1 (laboratory-confirmed coronavirus infection) and referred for a chest CT by a physician due to suspected community-acquired pneumonia caused by COVID-19; the maximum allowable period between laboratory verification and CT less ≤5 days. The observation period for each patient was at least 30 days from the CT scan in the outpatient clinic. We excluded patients without any typical coronavirus-associated chest CT changes, patients not assessed by the CT0–CT4 system, and patients with a negative polymerase chain reaction test as of 30/07/2020.

Equipment and CT protocol

The scanning was performed on 48 CT scanners, including Toshiba Aquilion 64 (Canon, Japan), Toshiba Aquilion CXL (Canon, Japan), and General Electric HiSpeed (GE, USA). For all studies, the standard protocol was used: voltage, 120 kV; tube current is adjusted automatically depending on the topogram; scanning direction—from the diaphragm to the lung apex; the field of view (FOV), 350 mm; slice thickness ≤ 1 mm; reconstruction kernel—lung, for Toshiba (Canon)—FC50/FC51/FC52/FC53, for GE—LUNG. Scanning was performed on breath-hold at an inspiration depth.

Evaluation of chest CT data

The initial assessment of the chest CT was performed using URIS by the outpatient CT center radiologists with 8–22 years of work experience. All the examinations were reviewed using URIS by on-duty experts of the Moscow Reference Radiology Center, with no other software used. Within 30 minutes after completing each primary protocol, an expert of the reference center with experience in thoracic radiology of ten years performed the audit and, if necessary, corrected the CT0–4 grade. Thus, the category was changed almost immediately, without saving the primary data. According to the audit reports, the percentage of discrepancies using the CT0–CT4 scale was up to 5%.

According to the Interim Methodological Recommendations of the Russian Society of Radiologists and the Russian Association of Ultrasound Diagnostics in Medicine, the so-called "empirical" visual scale is recommended to evaluate changes in the lungs detected by chest CT. It is based on a visual evaluation of the approximate volume of affected lung tissue [11]. This scale has five gradations, beginning at 0 and then with intervals of 25%. The Moscow Department of Health uses methodological recommendations, according to which the severity assessment of pulmonary lesions in COVID-19 should be based on the percentage of pulmonary tissue affected regardless of the semiotic phase of the process (ground-glass, crazy paving, consolidation) or their combination. This parameter is assessed separately for each lung. The category of changes is determined by the lung with the most extensive lesion (regardless of postoperative changes) [10].

Study hypotheses

The following questions were asked to conduct the study:

1. Is there a relationship between the CT0–CT4 grade in laboratory-confirmed patients and the risk of death?
2. Is there a relationship between the CT0–CT4 grade in laboratory-verified patients and survival rate?
3. Is there a relationship between the transition time for different grades and the initial CT0–CT4 category in the laboratory-confirmed patients?
4. Is there a relationship between the CT0–CT4 grade in laboratory-verified patients and the number of days from primary CT to hospitalization?

Statistical methods

The data analysis included all patients with a laboratory-confirmed diagnosis of COVID-19, for whom valid data was available on the dates of hospitalization and the dates of at least one CT scan. The result and date of the first CT scan that was used for the evaluation were taken as the baseline level and CT evaluation date: for 36,958 patients, this was the first CT scan; for 1,049 patients, the second CT scan; for 41 patients, the third CT scan; and for 3 patients, the fourth CT scan.

A logistic regression model was used to analyze data on patient deaths. Patient sex and age, as well as the CT severity grade, were used as the model factors. For each factor, the odds ratio (OR) of death, and the 95% confidence interval (CI) for OR, were estimated.

We applied the Kaplan–Meier method and Cox regression to analyze the time-to-event data (overall survival, time to CT deterioration, time from the baseline CT scan to hospitalization), patient sex and age, and the baseline CT severity grade as the model factors.

For the dependent variable, i.e., the number of hospitalizations, Poisson regression was performed using the above factors as covariates. The incidence rate ratio (IRR) and the corresponding 95% CI were estimated for each factor.

For data on the total duration of hospitalization (number of days) and the number of days from the date of baseline CT scan to laboratory confirmation of the diagnosis, a multivariate regression model was employed, which used sex, age, and CT severity grade as factors. For each factor, regression coefficient values were given with the 95% CI. Statistical analyses were performed using Stata 14 software.

RESULTS

A total of 240,985 patients were selected from UMIAS and URIS. On the other hand 202,934 patients were excluded from the study due to the lack of laboratory confirmation and data on the CT0–4 scale. The study sample consisted of 38,051 patients, including 21,888 men (57.5%) and 16,163 women (42.5%). The mean age was 50 ± 14.7 years. The total number of deaths was 182. The sampling process flowchart is shown in Figure 1. Following the baseline scan, most patients were classified as CT1 (Table 1).

For grade CT-4 patients, the risk of death was three times higher (p = 0.010). No statistically significant differences were found for CT-2 and CT-3 grades. Similar results were obtained in the overall survival analysis. In Kaplan–Meier survival curves, the survival rate of patients in the CT-3 category was almost three times lower (HR = 2.94) than that of the patients in the CT0-2 categories (Fig. 2).

The analysis of the time to chest CT deterioration by one or more grades relative to the baseline was performed. The results showed that the higher the baseline level, the lower the risk of deterioration (p < 0.001) (Fig. 3).

Also, it was found that the time to hospitalization decreased as the chest CT severity grade increased (p < 0.001) (Fig. 4).

In the analysis of the interval between the first and second CT scans (N = 12726), the mean time-lapse between them was 25.1 ± 21.9 days (95% CI 24.7–25.5), while the median time was 20 days. As for the time between the first and third CT scans (N = 2847), the time-lapse was 36.6 ± 28.8 days (95% of CI 35.4–37.5), while the median was 30 days. In the analysis of the interval between the first and fourth CT scans (N = 582), the mean time-lapse was 44.6 ± 26.5 days (95% of CI 42.4–46.7), while the median was 40 days.

Table 1. Distribution of patients by baseline CT0–CT4 grade

Baseline CT grade	Number of patients	Proportion (%)
0	8,112	21.3
1	18,704	49.2
2	8,180	21.5
3	2,773	7.3
4	282	0.7
Total	38,051	100.0

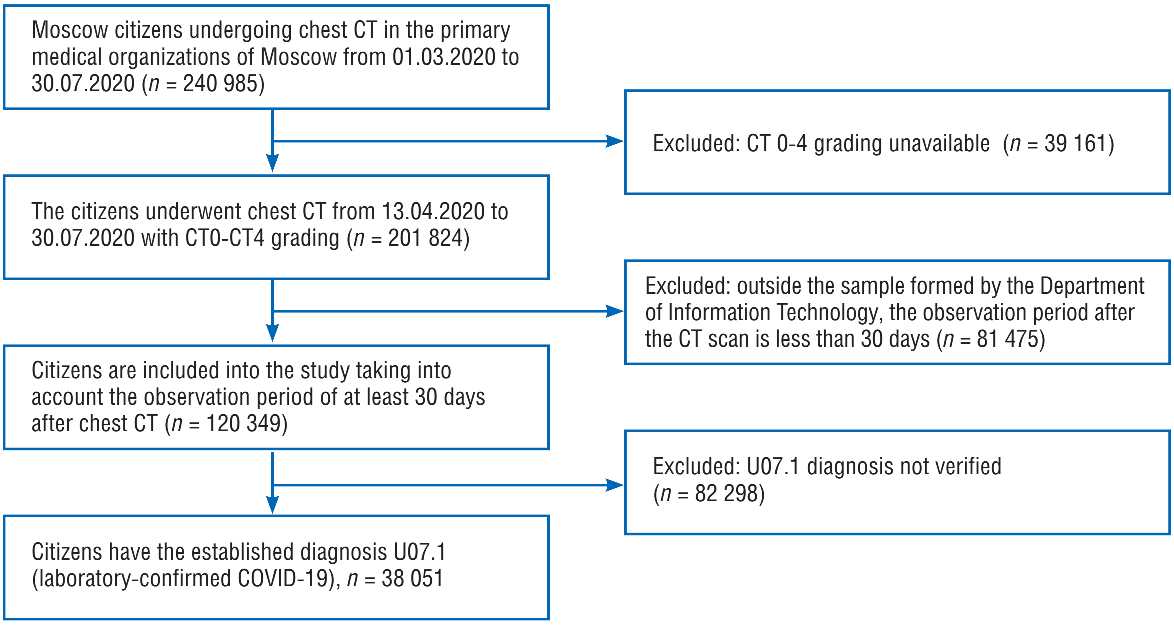

Figure 1. Sampling process flowchart.

Notes: CT — computed tomography; CT 0-4 — semi-quantitative visual scale of the pulmonary parenchyma damage

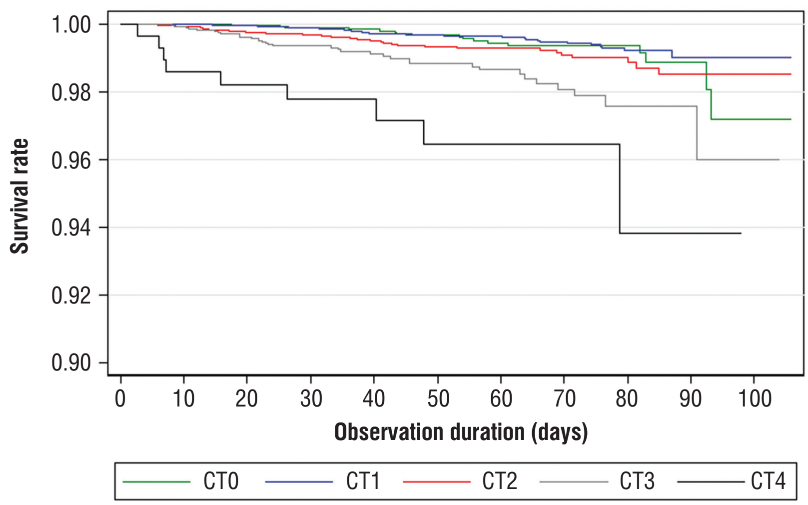

Figure 2. Overall survival curves for CT1-4 grades ($p < 0.0001$)

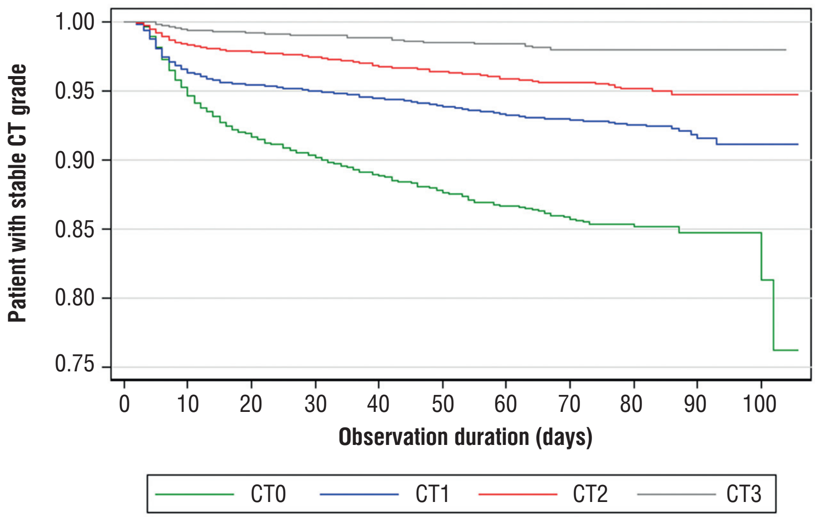

Figure 3. Kaplan–Meier curves for the time to deterioration by one or more grades relative to the baseline ($p < 0.0001$).

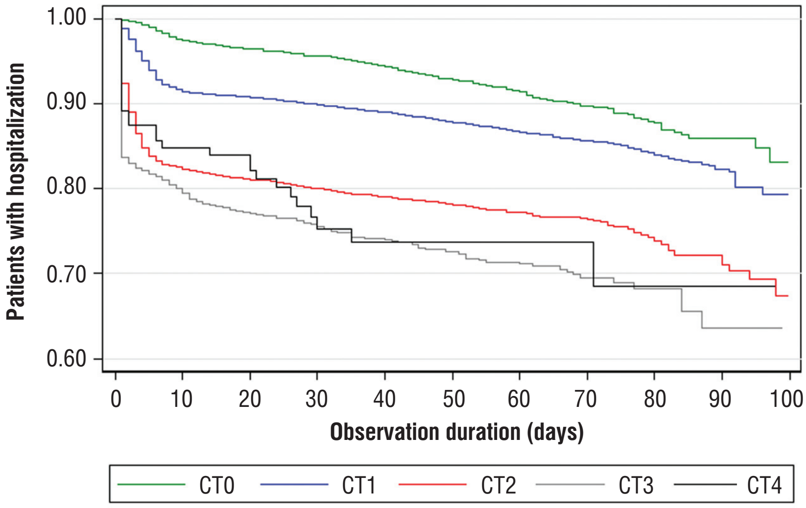

Figure 4. Kaplan–Meier curves for the time from the baseline CT to hospitalization ($p < 0.0001$)

DISCUSSION

This study showed that for grade CT-4 patients, the risk of death was three times higher than for grade CT-0 patients. According to Kaplan-Meier curves, the proportion surviving patients in the CT-3 category was almost 3 times lower (HR = 2.94) than in the CT0-CT2 categories. Also, it was found that the higher the baseline CT grade, the lower the risk of deterioration. In Fig. 3, the CT-3 curve is the most stable in time, while the CT-0, CT-1, and CT-2 curves tend to degrade. Therefore, the lighter grades (CT-0, CT-1, and CT-2) require the same attention as the severe disease, as there is a greater risk of disease progression. The time to hospitalization decreased as the chest CT severity grade increased.

It should be noted that the decision to hospitalize depends on the clinical status of the patient, peculiarities of the organization of a specialized bed fund, and legal acts. Also, patients could be hospitalized outside the observation period or hospitalized in facilities that are not connected to UMIAS. A higher all-cause mortality rate was registered in June, which may be due to the health system's workload and the imperfection of medical care algorithms in a complicated epidemiological situation.

Previously, we conducted a retrospective study that revealed that the probability of death increased progressively from CT-0 to CT-4. The patient's age and CT-0 to CT4 grade were statistically significantly associated with the time to death from COVID-19. When moving from one CT grade to the next, the risk increased by an average of 38% [12]. However, the earlier study included patients without laboratory confirmation of the coronavirus infection, the follow-up period was significantly shorter, and only the relationship between CT grade and deaths was evaluated. This study improves on previous results and is based on a larger sample with laboratory-confirmed diagnoses and more detailed information about the outcomes.

It was found that chest CT enables to detect pulmonary abnormalities that are characteristic of COVID-19 and grade them, which is in line with the results obtained by other authors [13,14]. Yuan et al. developed a prognostic model of deaths from COVID-19 that considers CT data but uses a comprehensive segment-by-segment evaluation of the CT images [15]. Errors may be accumulated due to the multicomponent semi-quantitative evaluation in the model. Other limitations include the long time required for data analysis and its complexity in routine practice. The proposed method of evaluating chest CT data is easily applicable in practice, correlates with the risk of death from all causes, overall survival, and risk of clinical deterioration.

Petrikov et al. revealed a relationship between increased lung involvement detected by CT and clinical deterioration in patients [16]. In a retrospective multicenter observational study by Xu et al., a multivariate analysis of 703 laboratory-confirmed cases of COVID-19 was performed, which showed a correlation between death and the presence of comorbidities, leukocytosis, lymphopenia, and severe lung impairment as shown by CT [17]. The authors proposed a visual segment-by-segment semi-quantitative scale to evaluate lung impairment, where the affected segment was evaluated as 1 point regardless of lesion morphology. When 14 segments (70%) or more were involved, the risk of death increased three times. Colombi et al. presented a quantitative assessment of the lung involvement using an open-source software, which showed a high correlation between preserved, well-ventilated lung tissue and the outcomes (transfer to the intensive care unit or death) [7]. In the study by Xiong et al., a small sample of 42 patients showed a positive correlation between the number of affected lung lobes at baseline and the risk of pulmonary infiltration progression [18]. The results of these studies are comparable to ours. The main differences include the use of the original CT0–4 scale and the examined populations. In our case, these were only patients who independently applied for medical care in the primary health care system.

Our study has several limitations. First, the data were analyzed retrospectively. However, this design allowed the study to include many patients with a long follow-up period. Second, the authors did not review the chest CT scans, possibly affecting the patient grading using the CT0–4 scale. Given the large sample size, the impact of borderline cases under- or overestimating the severity of lung impairment was minimized. Also, all studies were reviewed by on-duty medical experts from the Moscow Reference Radiology Center. Third, the large sample formed semi-automatically limited the validation possibilities. However, high statistical significance and literature analysis results support the validity of the findings in this study.

CONCLUSION

The visual CT0–4 scale can be used to predict outcomes (hospitalizations and deaths) in patients suspected of COVID-19 who underwent chest CT scans in primary health care.

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Сравнение частоты и характера внебольничных пневмоний до начала и во время эпидемии COVID-19 в многопрофильной больнице

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Обоснование. Вспышка коронавирусной инфекции 2019 года (COVID-19) быстро — всего за месяц — охватила весь мир. В диагностике этого заболевания помогает метод полимеразной цепной реакции (ПЦР), однако данный тест имеет ограничения, связанные с ложноотрицательными результатами, а также сроками выполнения. С учётом повышенного распространения инфекции компьютерная томография (КТ) органов грудной клетки (ОГК) может стать одной из основных методик в арсенале клинициста для раннего выявления COVID-19 у впервые обратившихся за медицинской помощью пациентов.

Цель — сравнение частоты внебольничных пневмоний и их характеристик по данным КТ в многопрофильной больнице Москвы до начала и во время эпидемии COVID-19 и изучение возможностей их своевременного выявления и дифференциального диагноза.

Материалы и методы. Проведён ретроспективный анализ результатов КТ грудной клетки пациентов Городской клинической больницы имени И.В. Давыдовского (Москва) за период с 1 по 17 апреля 2020 года. В исследование включены все пациенты с диагнозом вирусной пневмонии по заключению КТ. Всем пациентам с подозрением на вирусную пневмонию выполняли тестирование ПЦР. В качестве группы сравнения ретроспективно проанализированы данные КТ грудных клеток пациентов с подозрением на пневмонию за аналогичный промежуток 2019 г.

Результаты. С 1 по 17 апреля 2020 г. по данным КТ ОГК пневмония диагностирована в 140 случаях, из которых 65 (46,4%) описаны как вирусные, в сравнении с тем же периодом 2019 г. — 7 (10,3%) диагнозов вирусной пневмонии: наблюдается значимое увеличение частоты вирусных пневмоний (5,723; p <0,01). Результаты ПЦР-теста у пациентов с вирусной пневмонией по данным КТ: положительный — у 34 (52,3%), отрицательный — у 22 (33,8%), у 9 (13,9%) больных тест не проводился. При сравнении частоты обнаружения на КТ паттернов вирусной пневмонии у пациентов за одинаковый промежуток времени в 2019 и 2020 гг. не было обнаружено никаких достоверных различий. Вероятность COVID-19 по КТ-картине ОГК: средняя — 13,8%, высокая — 75,4%. Тяжесть вирусной пневмонии по данным КТ ОГК: лёгкая — 38,5%, среднетяжёлая — 46,2%, тяжёлая — 12,3%, крайне тяжёлая — 3,1%.

Заключение. КТ-диагностика COVID-19, в том числе при ложноотрицательных результатах ПЦР-тестов, позволяет вовремя изолировать пациента с подозрением на COVID-19, своевременно приступить к лечению и предотвратить дальнейшее распространение вирусной инфекции в условиях пандемии. Однако ввиду неспецифичности выявляемых изменений возможности КТ для идентификации поражения лёгких конкретными вирусными агентами ограничены.

Ключевые слова: COVID-19; компьютерная томография; пневмония; вирусная пневмония; полимеразная цепная реакция.

Как цитировать

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A comparison of the frequency and character of community-acquired pneumonia before and during the COVID-19 pandemic in a multi-specialty hospital

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BACKGROUND: The 2019 coronavirus disease (COVID-19) outbreak, first reported in Wuhan, China, quickly spread worldwide in just a month. Polymerase chain reaction (PCR) is used in the diagnosis of this disease, but this test has limitations related to false negative results and the time-consuming procedure. Under these conditions, chest computed tomography (CT) can become one of the main methods in the Clinician's Arsenal that is used for the early detection of COVID-19 in patients who first seek medical help.

AIMS: To compare the frequency of community-acquired pneumonia and its characteristics according to CT data in a multi-specialty Clinical Hospital I.V.Davydovskiy, State Moscow, before and during the COVID-19 epidemic and to study the possibilities of their timely detection and differential diagnosis.

MATERIALS AND METHODS: A retrospective analysis of chest CT scan results was performed in Davydovsky hospital, located in Moscow, for the period from April 1 to April 17, 2020. It included all patients diagnosed with viral pneumonia using the CT scan report. All patients with a suspected diagnosis of viral pneumonia underwent PCR testing on the first day of hospitalization and the results were analyzed. Retrospective analysis of chest CT data from patients admitted to the hospital with suspected pneumonia for the same period in 2019, taken as a comparison group, was performed.

RESULTS: From April 1 to April 17, 2020, according to the chest CT results, pneumonia was diagnosed in 140 cases, of which 65 (46.4%) were described as viral, compared with the same period in 2019; the diagnosis of seven cases of viral pneumonia (10.3%) was described as a significant increase in the cases of viral pneumonia (5.723; $p < 0.01$). Results of the PCR test in patients with viral pneumonia according to CT data were as follows: positive in 34 (52.3%) cases, negative in 22 (33.8%) cases, and 9 (13.9%) patients were not tested. When comparing the frequency of detection of viral pneumonia patterns in patients on CT for the same period of time in 2019 and 2020, no significant differences were found. The probability of COVID-19 due to results of chest CT was as follows: average, 13.8%; and high, 75.4%. The severity of viral pneumonia according to CT data was as follows: light, 38.5%; medium, 46.2%; severe, 12.3%; extremely severe, 3.1%. The following radiological phenomena were present in the group of patients with viral pneumonia according to the CT data: lymphadenopathy in 32.3%, hydrothorax in 21.5%, hydropericardium in 4.6%, and pulmonary hypertension in 21.5% of patients.

CONCLUSIONS: Our study showed that the rapid CT diagnosis of COVID-19, even with false negative results of PCR tests, can help to isolate patients with suspected COVID-19, start treatment on time, and prevent the further spread of the viral infection during pandemic. Nevertheless, due to the non-specificity of the revealed morphological picture, the possibilities of identifying lung lesions on CT caused by specific viral agents are limited.

Keywords: COVID-19; computed tomography; pneumonia; virus; polymerase chain reaction.

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某专科医院COVID-19流行前后社区获得性肺炎发生频率和性质比较

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论证：2019年中国武汉首次报道的2019冠状病毒病（COVID-19）在短短一个月内迅速席卷全球。聚合酶链反应（PCR）方法有助于诊断这种疾病，但这种检测有与假阴性结果，以及截止日期有限制。考虑到感染传播的增加，对胸部器官进行计算机断层扫描（CT）可以成为临床医生用于早期检测COVID-19患者的主要技术之一。

目的是根据莫斯科某专科医院COVID-19流行前和流行期间的CT资料，比较社区获得性肺炎的发生频率及其特征，并探讨其及时发现和鉴别诊断的可能性。

材料与方法。2020年4月1日至4月17日期间对I.V. Davydovsky City Clinical Hospital（莫斯科）患者胸部CT检查结果进行了回顾性分析。本研究纳入所有根据CT诊断为病毒性肺炎的患者。所有疑似病毒性肺炎患者均在住院第一天进行PCR检测。作为对照组，对2019年同期以疑似肺炎入院患者的胸部CT资料进行了回顾性分析。

结果。在2020年4月1日至4月17日期间，根据胸部器官计算机断层扫描，有140例确诊为肺炎，其中65例（46.4%）被描述为病毒性肺炎，与2019年同期相比，7例（10.3%）被诊断为病毒性肺炎：病毒性肺炎病例显著增加（5723例；p ＜ 0.01）。根据计算机断层扫描对病毒性肺炎患者进行PCR检测结果：34例（52.3%）为阳性，22例（33.8%）为阴性，未进行检测9例（13.9%）。比较2019年与2020年同期患者病毒性肺炎型CT检出频次，差异无统计学意义。胸部CT显示COVID-19的概率：平均概率为13.8%，高概率为75.4%。根据胸部CT检查病毒性肺炎的严重程度：轻度—38.5%，中度—46.2%，重度—12.3%，极重度—3.1%。在病毒性肺炎患者组中，根据CT资料，出现以下X线现象：淋巴结病为32.3%，胸水为21.5%，心包水为4.6%，肺动脉高压为21.5%。

结论。已经证明，以研究的相对速度对COVID-19进行CT诊断，并对获得的结果（包括PCR检测假阴性结果）进行解释，可以及时隔离疑似COVID-19患者，及时开始治疗，并防止病毒感染在大流行中进一步传播。然而，由于所检测到的形态学图像的非特异性，CT用特异性病毒制剂鉴别肺病变的可能性有限。

关键词：COVID-19；计算机断层扫描；肺炎；病毒性肺炎；聚合酶链反应

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BACKGROUND

In December 2019, a pneumonia outbreak caused by a new coronavirus occurred in China, which quickly spread worldwide [1].

Coronaviruses belong to the family of viruses that cause the common cold, as well as more serious respiratory diseases such as the severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), which have a mortality rate of approximately 10% and 37%, respectively [2, 3]. Both diseases (SARS and MERS) have been found to be zoogenous infections. The new coronavirus, designated by the International Committee on the Taxonomy of Viruses as severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2), caused the coronavirus disease (COronaVIrus Disease 2019, COVID-19) [4]. COVID-19 spread rapidly throughout China and then to other countries worldwide. Presently, COVID-19 has been declared a pandemic. This disease has also seriously affected the Russian Federation. It is known that most (up to 80%) infected patients may not have any obvious history of infection or clinical manifestations of the disease [5]. The rate of the disease spread confirms the high contagiousness of the new coronavirus, which is transmitted from person to person by aerosol (airborne and air-dust) and non-percutaneous routes [6].

The similarities of the clinical manifestations of SARS-CoV-2 infection with previous infections caused by betacoronaviruses have been noted [7]. The laboratory diagnosis of COVID-19 using the polymerase chain reaction (PCR) method is effective in identifying infected individuals and preventing the spread of the epidemic. However, it became obvious that patients had to wait for a long time (1–4 days) before getting the results of the PCR tests. In addition, it was established that PCR can give false negative results in a significant number of patients (up to 30%–40%), which negatively affects the epidemiological situation. A number of studies have shown that the sensitivity of chest computed tomography (CT) under conditions of the COVID-19 epidemic (in identifying patterns of lung tissue damage typical for this disease) can reach 80%–97% [8]. An accurate diagnosis of a viral pneumonia based on a chest CT scan enables to timely identify and quarantine infected patients, choose the approach for their treatment, and assess the dynamics of the disease. Due to the wide spread of the disease under the conditions of the epidemic and its frequent asymptomatic course, such patients may be admitted to multidisciplinary medical institutions (hospitals) with suspected community-acquired pneumonia. The timely isolation of such patients and their referral to specialized institutions depend on the early and accurate diagnosis of the COVID-19.

This study aimed to compare the incidence of community-acquired pneumonia and their characteristics according to CT data in a multi-specialty hospital in Moscow before and during the COVID-19 epidemic and to study the possibilities of their timely detection and differential diagnosis.

MATERIALS AND METHODS

Study design

A retrospective analysis of the chest CT scan results of patients from the I.V. Davydovsky Municipal Clinical Hospital of the Department of Health of Moscow was performed over the period from April 1 to April 17, 2020 (during the COVID-19 epidemic in Moscow).

Inclusion criteria

The study included all patients admitted to the hospital admission department with suspected community-acquired pneumonia. The reasons for hospitalization were fever >38.5°C, low-productive dry cough, chest pain, tachypnea, asthenia, headache, and diarrhea.

Description of the medical intervention

On the day 1 of hospitalization, all patients underwent testing by PCR and chest CT. The studies were performed using a Philips Inguenity computer tomograph (Netherlands) without the intravenous administration of a contrast agent, with the use of standard clinical protocols (slice thickness, 1 mm; tube current, 120 kV; product of current and time (mAs) was set automatically).

All CT images were evaluated in accordance with the international guidelines for the formation of standardized lung CT findings under conditions of the COVID-19 epidemic [9]. The criteria used to diagnose pneumonia of bacterial origin in the patients were the absence of areas of ground-glass opacity, presence of consolidation areas, and unilateral or bilateral lesions with or without hydrothorax. The criteria for diagnosing viral pneumonia on chest CT included characteristic radiographic patterns such as areas of ground-glass opacity of the lung tissue, mainly of peripheral localization; reticular crazy paving changes; and the presence or absence of consolidation areas. When describing lung changes, the probability of COVID-19 pneumonia (high, average, low) and the severity of changes in the lung parenchyma were calculated on a 4-point scale in accordance with the latest recommendations for the differential diagnosis of changes in thoracic organs of viral etiology [10].

We also analyzed the PCR results of patients with viral pneumonia diagnosed by CT in 2020.

Regarding the comparison group, we retrospectively analyzed the chest CT data of patients admitted to the hospital with suspected pneumonia for the same time period in 2019 in order to assess the dynamics of the total number of viral pneumonias and to identify morphological differences in pneumonias of viral etiology during CT studies performed a year ago. CT data of patients with viral pneumonia for 2020 and 2019 were compared according to the incidence of patterns such as ground-glass opacity symptoms, crazy paving symptoms, consolidation, and the nature of the lesion (unilateral or bilateral).

Within the group of patients with a history of viral pneumonia during the 2020 pandemic, we evaluated secondary radiological phenomena such as hydrothorax (fluid in the pleural cavities), hydropericardium (fluid in the pericardial cavity), pulmonary hypertension (dilatation of the pulmonary artery trunk by more than 30 mm), and lymphadenopathy (increase in the size of the lymph node by more than 10 mm along the short axis, quantitative).

Statistical analysis

For statistical analysis, we used the SPSS Statistics 23.0 software package (USA). Quantitative data are presented as mean values with standard deviation. Comparative analysis of groups was performed using Fisher's test and Chi-square test for contingency tables.

RESULTS

Study participants

From April 1 to April 17, 2020, 476 Chest CT examinations of the thoracic organs were performed at the I.V. Davydovsky Municipal Clinical Hospital. Pneumonia was diagnosed in 140 cases, including 65 (46.4%) cases that were classified as viral pneumonia and 75 (53.6%) cases as bacterial pneumonia, according to the CT results. During the same period in 2019, 309 chest CT examinations of the thoracic organs were performed, and pneumonia was detected in 68 patients; seven (10.3%) of these cases were classified as viral and 61 (89.7%) cases as bacterial.

Thus, there was an apparent increase in the number of viral pneumonia cases registered in April 2020 compared to the same period in 2019 (Fisher's exact test value 5.723; $p < 0.01$), which indicates a significant increase in the number of viral pneumonia cases due to pneumonia caused by COVID-19 in April 2020

Main results of the study

Analysis of CT results under conditions of the COVID-19 pandemic.

Most of the patients (95.4%) who were diagnosed with viral pneumonia according to CT were urgently isolated and transferred to specialized institutions that were repurposed for the treatment of patients with COVID-19. The only exceptions were patients (3.1%) who could not be transferred to specialized institutions for a number of reasons (concomitant pathology, severe condition, etc.).

Thirty-four (52.3%) of the 65 patients diagnosed with viral pneumonia by CT examination had a positive PCR test result for COVID-19, 22 (33.8%) patients had a negative result; and the CT examination was not performed in 9 (13.9%) patients for reasons beyond our control (refusal, visit to a medical institution at the place of residence) (**Fig. 1**).

The diagnosis of viral pneumonia by CT was done on average 2–3 days earlier than by PCR testing. Thus, CT has a high accuracy in diagnosing COVID-19 and can be used as a method for diagnosing COVID-19 in the general hospital.

CT patterns of lung changes in pneumonia associated and not associated with COVID-19

The CT scan of the thoracic organs showed a typical feature of viral pneumonia that is characteristic of the disease, namely extensive bilateral zones or foci of ground-glass opacities with a predominantly peripheral location and the presence or absence of consolidation zones, in all the 65 patients with COVID-19.

With the development of severe infectious diseases, SARS abnormalities of the lung parenchyma eventually spread to the central region and upper lobes of both sides [11, 12]. In our study, the progression of COVID-19 on CT images (13.8%) confirmed these findings (**Fig. 2**).

In the group of patients with COVID-19, the disease was predominantly peripheral (subpleural) and was noted in the middle and lower lung fields on the initial CT scan of the thoracic organs. Further studies revealed that pulmo-

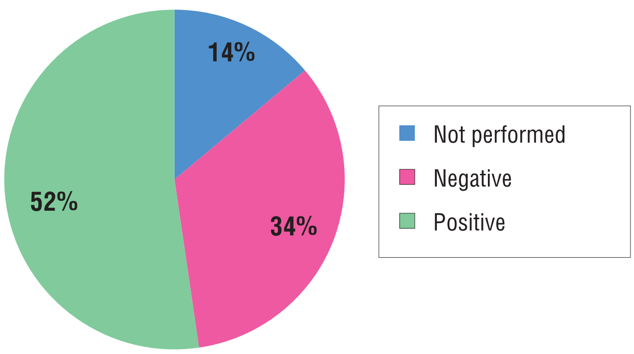

Fig. 1. PCR testing results of patients with viral pneumonia diagnosed by computed tomography.
Note. PCR — polymerase chain reaction.

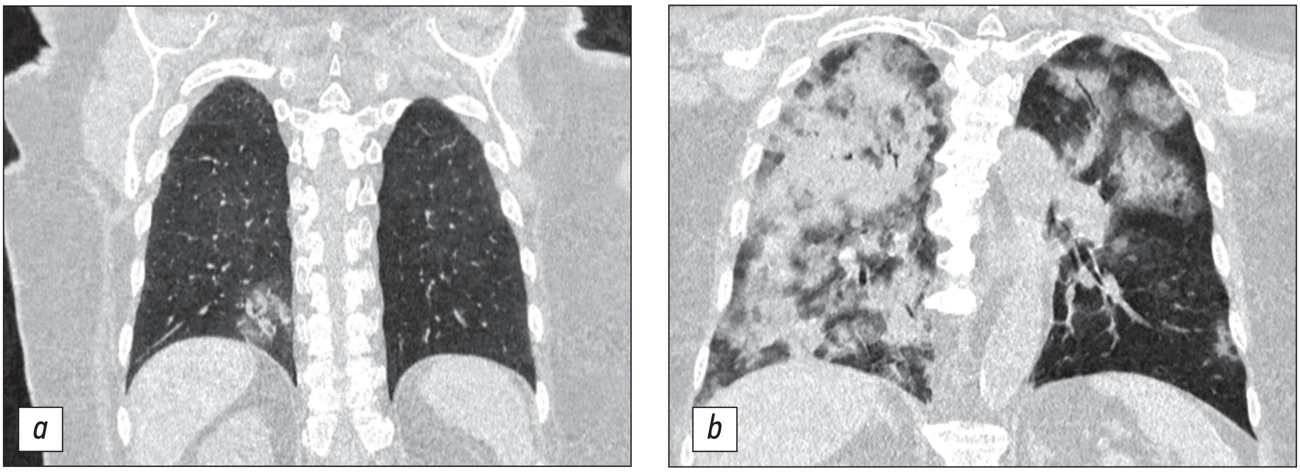

Fig. 2. Computed tomography of the chest organs of a patient who was admitted to the hospital for the first time with complaints of dry cough and fever: *a* — in the lower lobe of the right lung, a single area of ground-glass opacity can be seen; *b* — a bilateral lesion with the involvement of more than 75% of the lung parenchyma is noted on the control image obtained after five days, with general deterioration of the condition and the emergence of severe dyspnea, corresponding to an extremely severe course of the disease.

nary consolidation and fusion of infiltrates extended into the upper lobes of the organ as the disease progressed and affected them, as all five lobes of both lungs were affected in some patients, while "white" lungs were seen on CT. In our study group, an increase in the number of cases of ground-glass opacity and consolidation density indicated the progression of the disease, while the emergence of fibrosis and the resolution of the areas of ground-glass opacity or consolidation indicated improvement. However, the deformation of the bronchus due to fibrosis can lead to irreversible changes and affect the patient's respiratory function. These data suggest that lung lesions in COVID-19 may be present before the patients become symptomatic, and that CT should be performed promptly, even if the disease is asymptomatic.

Some patients had labored respiration on CT; therefore, obtaining perfect images during the final inhalation can be problematic. Thus, when reading CT images, radiologists should pay special attention to differentiate between areas of ground-glass opacity of the lung tissue and changes in the parenchyma caused by respiratory artifacts.

CT in the differential diagnosis of viral pneumonia

CT patterns of viral pneumonia are associated with the pathogenesis of viral infections. Most viral pneumonias have a similar pathogenesis [13]. Consequently, viral pneumonia caused by various viruses shows a similar presentation on chest CT images, which was revealed when we compared the CT images of chest organs of patients with viral pneumonias before the COVID-19 pandemic (April 2019) and during the pandemic (April 2020) (**Fig. 3**).

When comparing the CT detection frequency of viral pneumonia patterns in patients over the same period of time in 2019 and 2020, it was revealed that features such as the ground-glass opacity was registered in 100% of patients in both samples, crazy paving reticular changes were noted in 40% of patients in the 2020 sample and in 42% of patients in the 2019 sample, consolidation was registered in

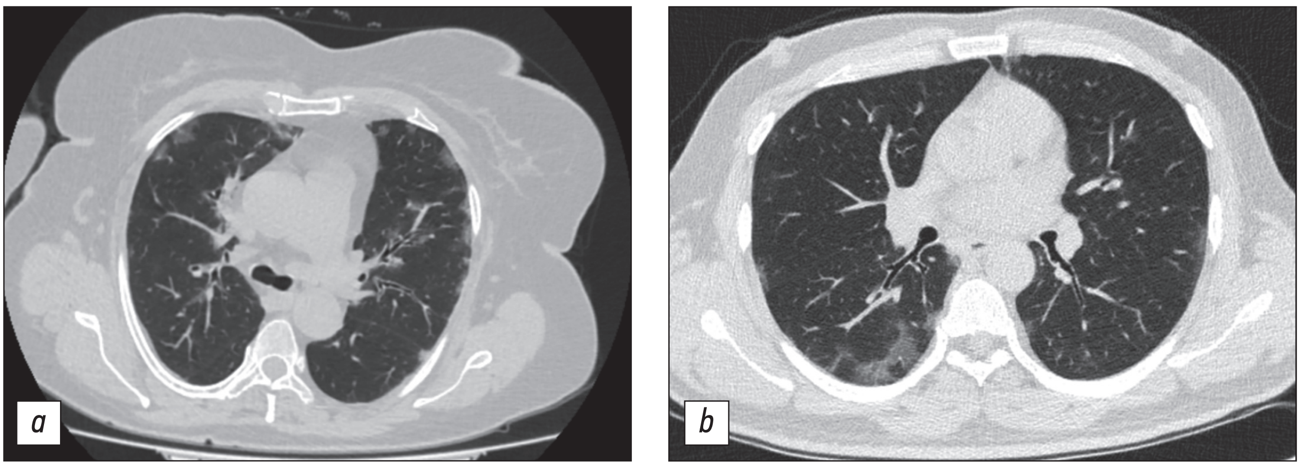

Fig. 3. Computed tomography of the chest organs; comparison of viral pneumonia images before and during the COVID-19 pandemic: *a* — multiple subpleural sites of ground-glass opacity of the lung tissue (April 2019); *b* — a similar presentation of an atypical pneumonia of viral origin (April 2020).

27% and 14% of patients, and bilateral lung damage was detected in 86.4% and 71.4% of cases in the 2020 and 2019 samples, respectively.

We also showed that all the aspects of viral pneumonia detected by primary CT examination in patients with COVID-19 (mainly peripheral ground-glass opacities of the lung tissue, vasodilatation, thickening of the interlobular and intralobular interstitium, and air bronchogram symptoms) are similar to the CT aspects in acute respiratory viral infections. In this case, all of the listed radiological characteristics of viral lung damage can be attributed to damage to the alveoli and interstitium of the organ, or its edema.

Mechanisms of lung damage in COVID-19-associated pneumonia

According to international studies, patients with severe pneumonia associated with COVID-19 may exhibit signs of systemic hyperinflammation, denoted by the general term macrophage-activation syndrome (MAS) or cytokine storm, also known as secondary hemophagocytic lymphohistiocytosis (sHLH) [14].

It is assumed that severe diffuse alveolar and interstitial inflammation also spreads to the nearby vasculature of the lungs, causing a MAS-like intrapulmonary inflammatory response that can lead to severe local vascular dysfunction, including microthrombosis and hemorrhage as manifestations of pulmonary intravascular coagulopathy.

Increased C-reactive protein levels and hyperferritinemia are the main indicators in the diagnosis of MAS/sHLH and are registered in many severe cases of COVID-19-associated pneumonia [15]. Other markers of MAS/sHLH include coagulopathy and liver dysfunctions that can also be detected in a subgroup of patients with pneumonia induced by COVID-19, suggesting a cytokine storm in patients with a combination of these parameters [16].

The assumptions about the possible presence of MAS/sHLH in patients with COVID-19-associated pneumonia are partially supported by our cases. Therefore, in several patients with severe COVID-19 pneumonia enrolled in this study, bronchoscopy revealed increased single pass petechiae in the presence of a hyperemic mucosa, which may partially indicate both active inflammation (in most patients, C-reactive protein levels are increased) and coagulopathy in presence of impaired liver functions.

The pathogenic mechanisms of lung damage in COVID-19 require a more detailed study and the comparison of CT images of patients with COVID-19 with the results of bronchoscopy, coagulogram, and blood biochemical parameters, which would explain the mechanism of formation of ground-glass opacity sites of the lung tissue, as well as rapid changes of the thoracic organs based on CT results.

Probability and severity of COVID-19

The probability of COVID-19 according to the chest organs CT presentation of viral pneumonia (65 cases) was estimated as average for 13.8% of cases and high for 86.2% of cases (**Fig. 4**).

The severity of viral pneumonia according to the CT of the thoracic organs was mild in 38.5% of cases (**Fig. 5, *a***), moderate in 46.2% (**Fig. 5, *b***), severe in 12.3% (**Fig. 5, *c***), and extremely severe in 3.1% of cases (**Fig. 5, *d***).

Concomitant morphological phenomena have been noted, such as:

- lymphadenopathy in 7.7% of cases, including only quantitative in 24.6% of cases, absent in 66.2% of cases;
- unilateral hydrothorax in 7.7%, bilateral in 13.8%, and absent in 78.5% of cases;

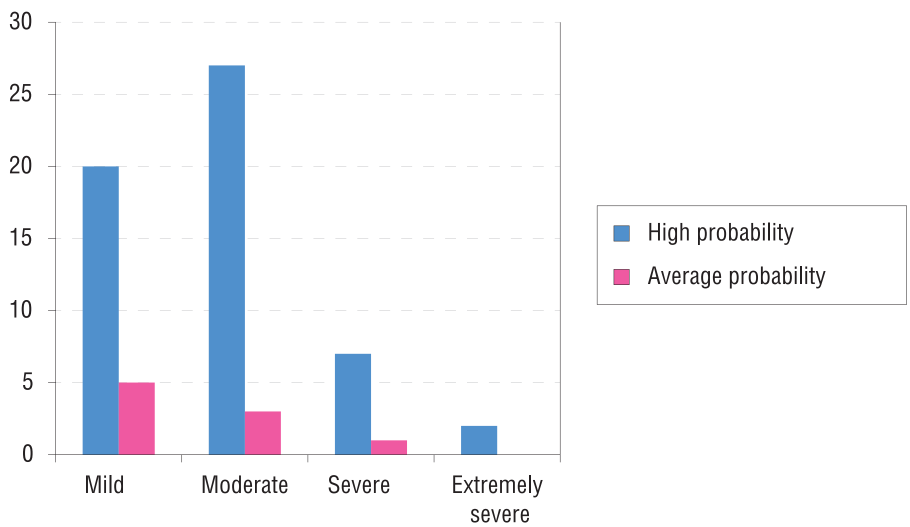

Fig. 4. Distribution of patients with a high and an average probability of COVID-19 according to the CT of the thoracic organs and depending on the disease severity.

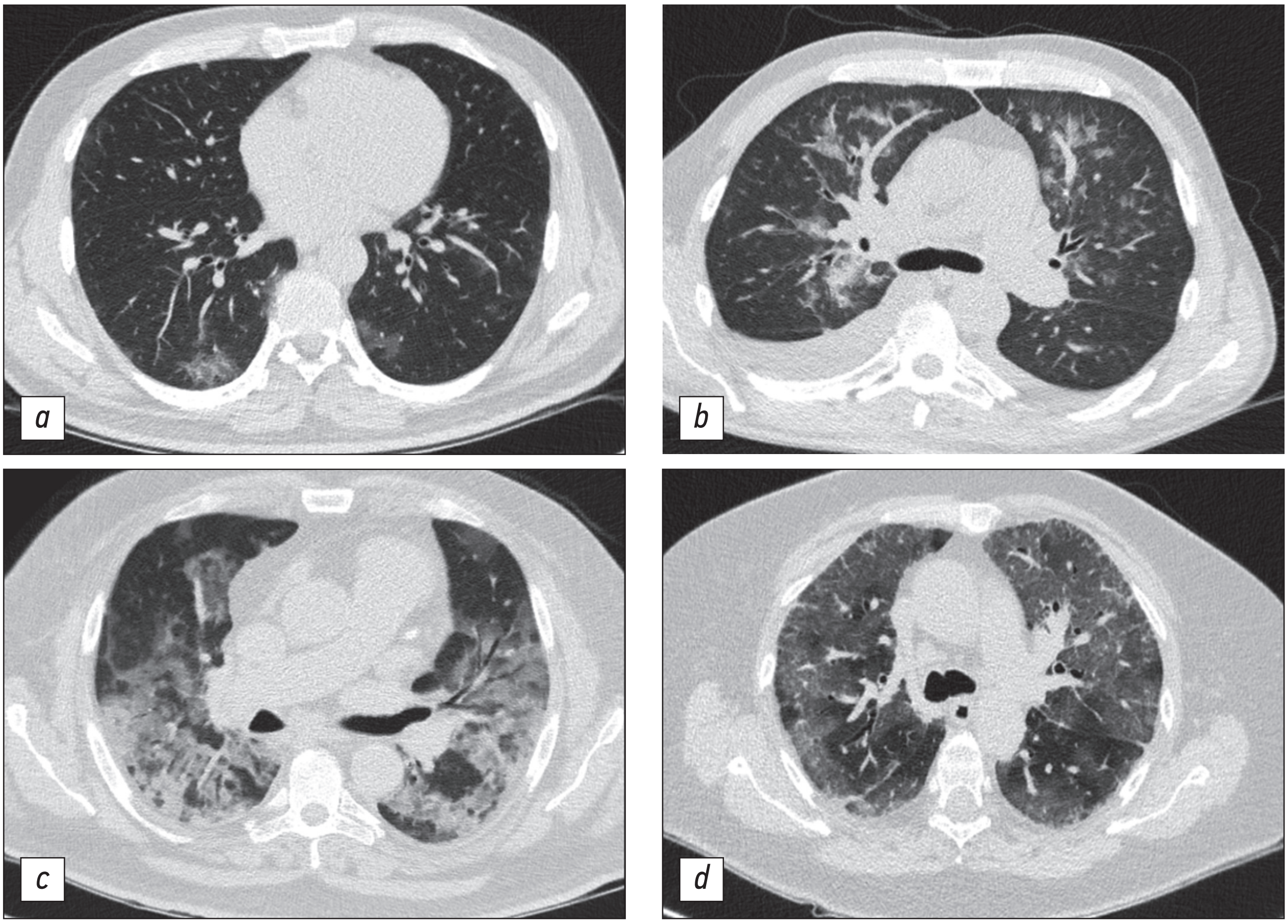

Fig. 5. Viral pneumonia severity according to the computed tomography of the thoracic organs: *a* — mild changes (CT-1), involvement of the lung parenchyma by ≤25%; *b* — moderate changes (CT-2), involvement of the lung parenchyma by 25%–50%; *c* — severe changes (CT-3), involvement of the lung parenchyma by 50%–75%; *d* — extremely severe and critical changes (CT-4), involvement of the lung parenchyma by ≥75%.

- hydropericardium in 4.6% of cases and absent in 95.4% of cases;
- pulmonary hypertension in 21.5% and absent in 78.5% of cases.

The dynamics of viral pneumonia was not traced in 86.2% of cases, and was negative in 13.8% of cases.

Viral pneumonia resulted in improvement (discharge) in 1.5%, transfer to a COVID-19 hospital in 95.4%, and a lethal outcome in 3.1% of cases.

It should be noted that, statistically significantly, in more severe cases of viral pneumonia, radiological phenomena such as hydrothorax (bilateral or unilateral) and pulmonary hypertension (Kruskal–Wallis test, where $p = 0.031$ and $p = 0.026$, respectively) were found on CT of the thoracic organs. In the pairwise comparison of the groups with viral pneumonia of varying severity and these phenomena using Fisher's test, a statistically more frequent occurrence of pulmonary hypertension was determined in the moderate (11 out of 30) compared to the mild (0 out of 25) X-ray presentations of pneumonia ($p < 0.01$), and hydrothorax was more often detected in the moderate (8 out of 30) and severe (4 out of 8) cases by CT ($p < 0.01$).

Finally, the severity of viral pneumonia has a statistically significant effect on the course of the disease, as negative changes are more common in cases of severe (4 out of 8) pneumonia compared to moderate (2 out of 30; Fisher's test, $p < 0.01$) and mild (3 out of 25; Fisher's test, $p < 0.05$) cases.

CONCLUSION

The number of viral pneumonias detected in April 2020 was significantly higher than that which was detected in the same period in 2019, due to the emergence of a new viral agent (COVID-19).

In one-third of patients with a characteristic CT presentation of viral pneumonia, PCR tests showed negative results, which indicates possible false negative test results and the need for a CT scan of the thoracic organs in combination with PCR testing.

The results of CT under conditions of the COVID-19 pandemic in 2020 coincided partially with the results of CT of other viral pneumonias diagnosed in April 2019. In 65 cases of viral pneumonia, it was possible to demonstrate that a more severe CT presentation upon admission determines a greater probability of developing the disease by an

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unfavorable scenario (negative dynamics), for example, in the group of patients with severe lung damage, two lethal outcomes were recorded. In addition, CT scans revealed radiological phenomena such as hydrothorax (bilateral or unilateral) and pulmonary hypertension significantly more often in severe cases of viral pneumonia. However, the ability of CT to identify lung damage due to specific viral agents is limited, since the X-ray CT presentation of lung damage in COVID-19 overlaps with the results of the CT of the thoracic organs in patients infected with other respiratory viruses.

Our study showed that CT, combined with clinical and anamnestic data, and PCR testing, can be useful as a standard method for diagnosing COVID-19, especially in a general hospital. CT diagnosis of COVID-19, characterized by the relative speed of the examination and the interpretation of the results obtained, even with the false negative results of the PCR tests, enables to timely quarantine patients with suspected COVID-19, prescribe treatment, and prevent the further spread of the viral infection during the pandemic, which helps to optimize patient management.

ADDITIONAL INFO

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Authors contribution. S.A. Yaremenko — manuscript writing, analysis and expert evaluation of results; N.A. Rucheva — expert assessment of results; K.N. Zhuravlev — search for publications, review part editing; V.E. Sinitsyn — systematization and final editing of the article. All authors made a significant contribution to the study and preparation of the article, read and approved the final version before publication.

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MosMedData: датасет 1110 компьютерных томографий органов грудной клетки, выполненных во время эпидемии COVID-19

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ГБУЗ «Научно-практический клинический центр диагностики и телемедицинских технологий Департамента здравоохранения города Москвы», Москва, Российская Федерация

В условиях пандемии COVID-19 и лавинообразного роста числа выполняемых компьютерных томографий (КТ) лёгких особое значение приобретают методы автоматизации процесса анализа изображений, использование которых позволит повысить производительность и минимизировать ошибки. Создание качественных наборов данных необходимо для развития технологий искусственного интеллекта. Алгоритмы искусственного интеллекта обладают достаточной точностью для диагностики COVID-19. Данный датасет[1] содержит как анонимизированные компьютерные томограммы (КТ) лёгких человека с признаками COVID-19, так и нормальные исследования грудной клетки. Некоторая часть исследований была размечена с использованием бинарных пиксельных масок представляющих интерес областей (например, зон консолидации и уплотнений по типу матового стекла). КТ-данные были получены в период с 1 марта 2020 г. по 25 апреля 2020 г. и предоставлены муниципальными больницами г. Москвы (Россия)[2]. Предлагаемый набор данных лицензирован Creative Commons Attribution-NonCommercial-NoDerivs 3.0 Unported (CC BY-NC-ND 3.0).

Ключевые слова: искусственный интеллект; COVID-19; машинное обучение; датасет; КТ; органы грудной клетки.

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DOI: https://doi.org/10.17816/DD46826

[1] Data set — *набор данных (set of data)*, обработанная и структурированная информация, обычно в табличном виде, пригодная для статистического анализа, визуализации и обработки алгоритмами машинного обучения.
[2] Постоянная ссылка: https://mosmed.ai/datasets/covid19_1110.

Рукопись получена: 12.10.2020 **Рукопись одобрена:** 11.12.2020 **Опубликована:** 21.12.2020

MosMedData: data set of 1110 chest CT scans performed during the COVID-19 epidemic

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With the ongoing COVID-19 pandemic decreasing availability of polymerase chain reaction with reverse transcription and the snowballing growth of medical imaging, especially the number of chest computed tomography (CT) scans being performed, methods to augment and automate the image analysis, increasing productivity and minimizing human error are of particular importance. The creation of high-quality datasets is essential for the development and validation of artificial intelligence algorithms. Such technologies have sufficient accuracy in diagnosing COVID-19 in medical imaging. The presented large-scale dataset contains anonymized human CT scans with COVID-19 features as well as normal studies. Some studies were tagged by radiologists using binary pixel masks of regions of interest (e.g., characteristic areas of consolidation and ground-glass opacities). CT data were acquired between March 1, 2020, and April 25, 2020, and provided by municipal hospitals in Moscow, Russia. The presented dataset is licensed under Creative Commons Attribution-NonCommercial-NoDerivs 3.0 Unported (CC BY-NC-ND 3.0).

Keywords: artificial intelligence; COVID-19; machine learning; dataset; CT, chest.

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MosMedData: COVID-19疫情期间进行的1110次胸部CT扫描数据集

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在COVID-19大流行和雪崩式增加肺部计算机断层扫描的数量背景下，图像分析过程的自动化方法特别重要，使用这种方法将提高生产率并减少错误。高质量数据集的创建是人工智能技术发展的必要条件。人工智能算法对COVID-19的诊断具有足够的准确性。该数据集1包含有COVID-19征象的患者的匿名肺部CT图像和正常的胸部检查。一些研究使用感兴趣区域的二元像素遮罩进行标记（例如，肺结节整合和磨砂玻璃结节）。获取2020年3月1日至2020年4月25日期间的CT数据，提供给莫斯科市医院（俄罗斯）2。建议的数据集由Creative Commons Attribution-NonCommercial-NoDerivs 3.0 Unported授权（CC BY-NC-ND 3.0）。

关键词：人工智能；COVID-19；机器学习；数据集；CT；胸部器官

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DOI: https://doi.org/10.17816/DD46826

[1] Data set是数据集（set of data），经过处理的结构化信息，通常以表格形式，适用于机器学习算法的统计分析、可视化和处理。
[2] 永久链接：https://mosmed.ai/datasets/covid19_1110

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BACKGROUND

During the COVID-19 pandemic, most countries encountered a huge increase in the burden on health structures. More than ever, this situation required the careful use of financial and human resources. Unfortunately, the preventive measures taken in health facilities are not always sufficient to avoid the loss of health workers. The loss of trained specialists in emergency care, radiology, etc. is of particular concern. Computed tomography (CT) is considered to be the key tool for the diagnosis of pneumonia and the assessment of its progression. CT is performed in outpatient settings and is intended for patients with acute respiratory symptoms, as well as for those initially diagnosed with viral pneumonia requiring follow-up, and capable of recovering at home (under observation using telemedical technologies).

In in-patient facilities, CT is used for making the primary and differential diagnosis, assessing disease progression, and determining whether a patient should be admitted to the intensive care unit or discharged [1,3,4]. The increasing use of CTs is placing a heavy burden on the health care system. For example, in Moscow, the network of municipal outpatient CT centers is conducting approximately 90 examinations per CT scanner per day (with up to 163 examinations per day). Therefore, to standardize and streamline the clinical decision-making, specialists developed a classification model that, along with other symptoms, evaluates the severity of pulmonary tissue anomalies observed on CT scans (see Table 2). This classification according to the pulmonary parenchyma lesion volume in chest CT allows to predict lethal outcomes in COVID-19 [9]. Professional burnout and high risks of death among health professionals require image analysis automation, which will increase productivity and minimize errors [8]. Preliminary data show that artificial intelligence (AI) algorithms have sufficient accuracy for diagnosing COVID-19 (sensitivity: 90%, specificity: 96%, AUC: 0.96, overall accuracy: 76.37–98.26). [6,10].

MATERIALS AND METHODS

Chest CT was performed on 42 CT scanners of the same model Toshiba Aquilion 64 (Canon Medical Systems, Japan). All examinations were performed according to the standard methods and protocols recommended by the manufacturer (Table 1):

One examination refers to a single patient and includes one three-dimensional reconstruction. The inclusion criteria were as follows: patient visit to an outpatient clinic, reorganized as Outpatient Computed Tomography Center during the pandemic as well as referral for a chest CT from the general practitioner under the obligatory health insurance. The criteria for exclusion from the study included pregnancy and age under 18 years. Patients with blood oxygenation less than 93%, identified before the CT scan, were removed from the study and sent to be hospitalized by the ambulance service.

The dataset was developed in five stages as discussed below.

DATA COLLECTION

Data collection was conducted in the period from March 1 to April 25, 2020 in the outpatient clinics of Moscow City Health Care (Table 3).

This dataset (1110 studies) contains anonymized human lung CT scans (CT scans) with signs of COVID-19 (CT1-CT4) and without signs of COVID-19 (CT0) (Figure 1). Sample characteristics: 1110 individuals, of whom 42% were males, 56% females, 2% other/unknown; aged 18 to 97 years old, median age 47.

At the first stage, all the examinations (n=1110) were distributed into five categories according to the classification (Table 2). The number of cases by categories: CT-0, 254 (22.8%); CT-1, 684 (61.6%); CT-2, 125 (11.3%); CT-3, 45 (4.1%); and CT-4, 2 (0.2%). Second, each study was saved in the NIfTI format and archived in the Gzip archive. During this process, only every 10th image (Instance) was saved in the final study file.

A small number of the CT scans ($n = 50$) was tagged by specialists from the Research and Practical Clinical Center for Diagnostics and Telemedicine Technologies of the Moscow Department of Health. During the markup, positive (white) pixels on the corresponding binary pixel mask were selected for each of the images. The obtained masks were saved in NIfTI format and then converted to the Gzip archives. MedSeg® annotation software (© 2020 Artificial Intelligence AS) was used to create the binary masks.

This software was used to tag only COVID-19 lesions, including ground-glass opacities, consolidation, small vessels, and bronchioles. The density thresholds for tagging were from –700 HU to –130 HU, but it could differ depending on the breathing depth. We excluded large vessels and bronchi, visually unchanged pulmonary parenchyma, motion artifacts (respiratory due to cough and respiratory failure), gravitational changes (if it was possible to reliably differentiate them), calcifications, and pleural effusion.

All chest CT scans used in the dataset have passed an independent external audit by radiologists from the Research and Practical Clinical Center for Diagnostics and

Table 1. Methods of scanning, reconstructing images, and saving the database

Parameter set	Feature	Meaning and comment
Equipment	CT-scanner	Toshiba Aquilion 64 (Canon Medical Systems, Japan)
	Number of slices	64
Patients	Patient positioning	Gantry centered at the thorax Table height and alignment are adjusted such that the middle clavicular line is in the isocenter Hands above the head Instructions for breathing Patient education and breathing instruction before scanning
	Clothing and foreign objects	All foreign objects should be removed from the scan area, including jewelry and chains around the neck. Underwear is acceptable.
Patients	Localizer/scout	- Was conducted at the chest level to limit the scanning to the lung range. - Was performed to find additional foreign objects at the scan level that could impair the image quality. - Breath-hold scan at breathing depth.
	Scanning range	The entire volume of the lungs, including 5 cm above and 5 cm below the lungs.
	Breathing phase	CT scan with breath-holding at inspiration depth.
	Field of view (FOV)	- Not less than 1 cm from the ribs (from 350 to 500 mm). - The breasts were included in the scanning area, but could be partially excluded from the field of view
Medical staff	Technician	He was in the control room and not in contact with the patient. Face-to-face contact with the positioning assistant was minimized for safety reasons.
	Stacker	The positioning assistant is a medical officer of the Radiology Department who was transferred from the mammography X-ray technicians to the CT room in the form of additional personnel during the epidemic according to the order of the Moscow Department of Health. He was located in the scanner room (assisting with patient and table positioning) and in the corridor (during scanning). He was in contact with the patient.
Scanning protocol and image reconstruction, viewing, and interpretation	Gentri tilt	no
	Scan duration	≤ 10 seconds
	Contrast enhancement	no
	Oral contrast	no
	Voltage	120 kV
	Current	Automatic power modulation system «Sure exp.3D», built into the CT manufacturer. The system automatically adjusted the current strength to achieve a noise level of 10 HU for 5.0 mm-thick slices thick in the range of 80–500 mA. XY modulation - on
	Rotation speed	0,5 s
	Pitch	95,0
	Recon process	QDS+

Parameter set	Feature	Meaning and comment
Scanning protocol and image reconstruction, viewing, and interpretation	Number of CT series reconstructed	2 (with pulmonary and soft tissue kernel[3])
	Convolution kernel for soft tissues	FC07 or FC18
	Convolution kernel for lungs	FC51
	Slice thickness	1.0 mm (same for both kernels)
	Increment	0.8 mm (same for both kernels)
	Iterative reconstruction	AIDR 3D was availible in only 5 tomographs, the rest - without iterative reconstruction algorithms - used FBP (filtered back projection).
	Software used for CT interpretation	AGFA Enterprise 8.0 Vitrea FX
	Maximum Intensity Projections (MIP), Minimum Intensity Projections (MIP), and Multiplanar Reconstruction (MPR)	Maximum Intensity Projections (MIP), Minimum Intensity Projections (MIP), and Multiplanar Reconstruction were used
	Artificial Intelligence Algorithms	They were used, but not for all examinations. In the case of machine learning, algorithms created an additional image series for the radiologist, highlighting the COVID-19 lung lesion. COVID-19 was shown as red rectangles, attracting the attention of the doctor. In addition, a summarized three-dimensional reconstruction of the lungs with red regions of interest was available. Quantitative information to estimate the degree of lung damage was not presented.
	Report turnaround time	from 10 min to 3 hours. In rare cases 24 hours.
	Protocol standartization	The structured report template was formed and regulated in the methodical recommendations, as well as implemented in the Unified Radiological Information Service, used for study reporting in the outpatient clinics.
	COVID-19 classification	Classification by the CT0-CT4 scale was used (see table).
	Second opinion	For 90% of all CT examinations from outpatient clinics, a second reading was performed.
	Effective dose calculation	DLP data from the automatically created DoseReport CT series were used. In the Russian Federation, according to the methodological guidelines (MU 2.6.1.2944-11) «Control of Effective Patient Doses during Medical Radiology», the effective dose is calculated by multiplying DLP by 0.017 (anatomic location-based index).
Dataset	Data acquisition	Unified Radiological Information Service, including AGFA Enterprise 8.0
	Initial data collection format	DICOM 3.0
	Plane	Axial

Parameter set	Feature	Meaning and comment
Data base	Slice thickness	1.0 mm
	Increment	8.0 mm (as every 10th slice is saved)
	Export file extenstion	NIfTI
	Annotation software in the form of binary masks with lung lesions	MedSeg® (© 2020 Artificial Intelligence AS)

Notes: CT — computed tomography; CT-1 – CT-4 — the degree of lung damage based on CT results; RR — respiratory movements rate; FiO_2 — oxygen concentration; SpO_2 — blood oxygen saturation.

Table 2. Lung lesion grading in COVID-19 and routing rules

Severity	CT category	Clinical Data	Decision
Zero	CT-0 Not consistent with pneumonia (including COVID-19).	–	Inform the attending physician. Refer to a specialist.
Mild	CT-1 Ground-glass opacities. Pulmonary parenchymal involvement =<25% OR absence of CT signs in the presence of typical clinical manifestations and relevant epidemiological history.	A. t <38.0ºC B. RR <20/min C. SpO_2 >95%	Follow-up at home using telemedicine technologies (mandatory telemonitoring)
Moderate	CT-2 Ground-glass opacities. Pulmonary parenchymal involvement 25–50%	A. t >38.5ºC B. RR 20–30/min C. SpO_2 95%	Follow-up at home by a primary care physician
Severe	CT-3 Ground-glass opacities. Pulmonary consolidation. Pulmonary parenchymal involvement of 50–75%. Lung involvement increased in 24–48 hours by 50% with respiratory impairment per the follow-up studies.	One or more signs on the background of fever: A. t >38,5ºC B. RR ≥30/min C. SpO_2 ≤95% D. Partial pressure of oxygen (PaO_2)/ Fraction of inspired oxygen (FiO_2) ≤300 mmHg (1 mmHg=0,133 kPa)	Immediate admission to a COVID specialized hospital. In a hospital setting: immediate transfer to the intensive care and resuscitation unit. Emergency computed tomography (if not done before).
Critical	CT-4 Diffuse ground-glass opacities with consolidations and reticular changes. Hydrothorax (bilateral, more on the left). Pulmonary parenchymal involvement >=75%.	Signs of shock, multiple organ failure, and respiratory failure.	Emergency medical care. Immediate admission to a specialized hospital for patients diagnosed with COVID-19. In a hospital setting: immediate transfer to the intensive care and resuscitation unit. Emergency computed tomography (if not done before and when patient status allows for it).

Notes: CT — computed tomography; CT-1 – CT-4 — the degree of lung damage based on CT results; RR — respiratory movements rate; FiO_2 — oxygen concentration; SpO_2 — blood oxygen saturation.

Table 3: List of medical organizations where CT data was collected

Municipal Hospital (MH) № 19 Department of Health Care of Moscow	MH № 214	MH № 52
MH № 23	MH № 6	Diagnostic Center № 5
MH № 3	MH № 209	MH № 9
MH № 62	Diagnostic Center № 4	MH № 218
MH № 175	MH № 212	MH № 170
MH № 191	MH № 8	M. P. Conchalovsky hospital (outpatient and in-patient care)
MH № 195	MH № 64	MH № 134
MH № 115	Pediatric Diagnostic Center № 1	MH № 67
Diagnostic Center № 121	MH № 36	MH № 68
Diagnostic Center № 2	MH № 11	MH № 180
MH № 45	MH № 5	MH № 5
MH № 2	Moscow Research and Practical Center for Tuberculosis Control of the South-East Moscow District	MH № 46
MH № 166	Moscow Research and Practical Center for Tuberculosis Control of the Central and West Moscow Districts	MH № 12
MH № 220	MH № 66	Diagnostic Center № 3

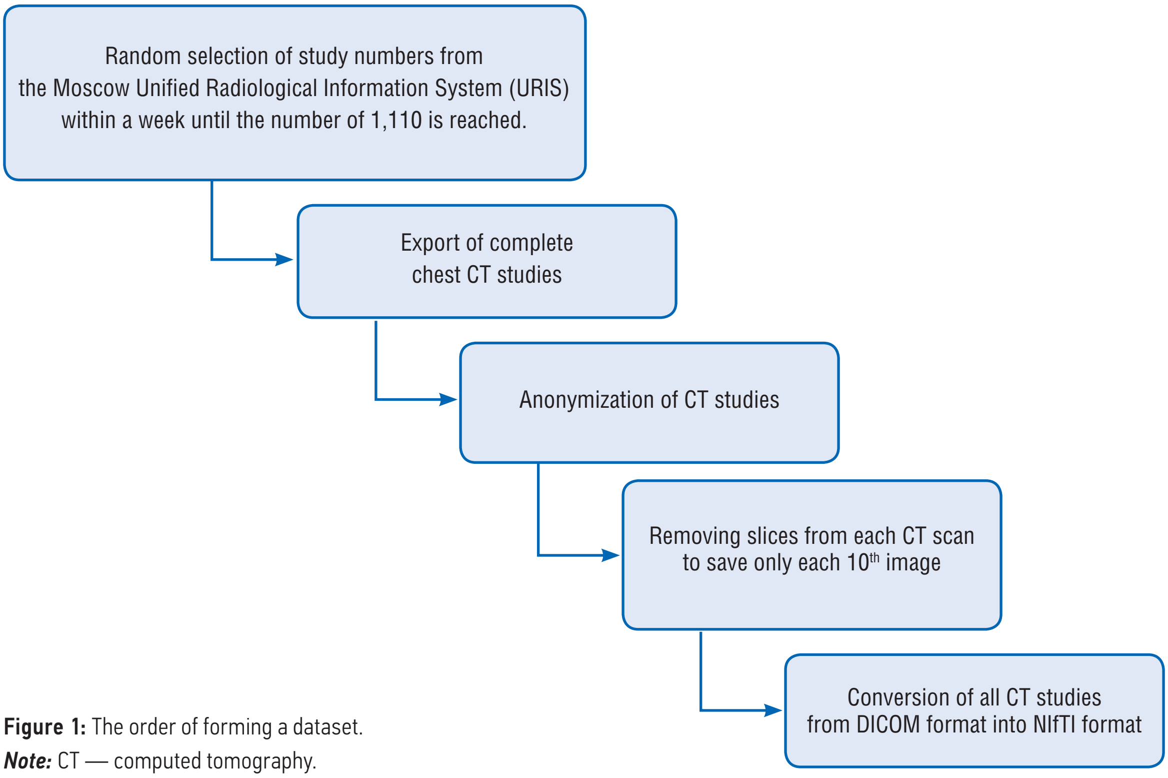

Figure 1: The order of forming a dataset.
Note: CT — computed tomography.

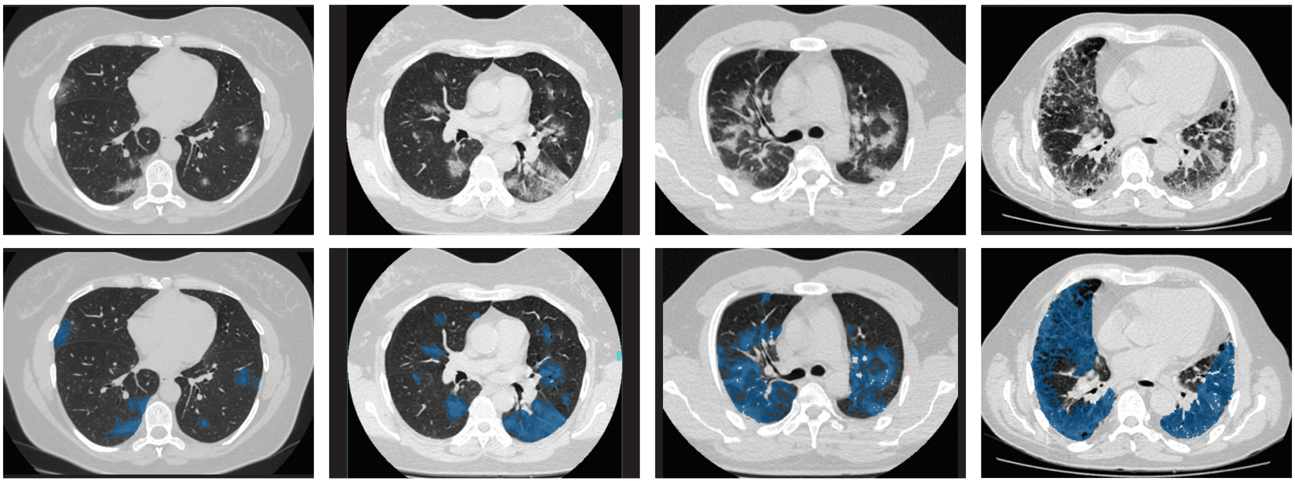

Figure 2: Examples of chest CT scans of patients with varying degrees of COVID-19 severity. Left to right, upper row: axial CT slices of patients with COVID-19 from mild (CT-1) to critical (CT-4) severity. Left to right, lower row: same CT data after tagging.

Telemedicine Technologies of the Moscow Department of Health, the opinion of which was accepted as final to assess the severity of COVID-19 lung damage according to the adopted classification (CT0-CT4). These data were available in URIS in a structured form to constitute the final table of assessment results. Thus, all the studies were evaluated by at least two specialists. In addition, 50 studies were evaluated by three specialists, as they were annotated using the external MedSeg software.

The data set is intended for training, calibration, and the independent evaluation of AI algorithms (computer vision) [7]. The COVID-19 AI algorithms (computer vision) will help in the fight against this disease:

1. Examine patients in outpatient facilities for fast and consistent routing (including those based on CT0-4 criteria).
2. Prioritize studies with COVID-19 features in a worklist.
3. Perform a rapid and qualitative assessment of abnormal changes by comparing several studies.
4. Minimize the risk of errors and missed anomalies.

Currently, there is a wide range of publicly available COVID-19 data sets [2,5]. However, this should not be seen as an obstacle, since the development of artificial intelligence algorithms requires large amounts of qualitative clinical information that are representative of real patient populations. In addition, Artificial Intelligence algorithms should be tested using new data sets that were not used in the training and calibration stages. The more data available in open sources, the better for developers. The available data sets are relatively small and rarely contain additional information such as tags and/or binary masks for regions of interest (ROI).

How to use the dataset

Permanent link: https://mosmed.ai/datasets/covid19_1110. This data set is licensed under the Creative Commons Attribution-NonCommercial-NoDerivs 3.0 Unported (CC BY-NC-ND 3.0) license.

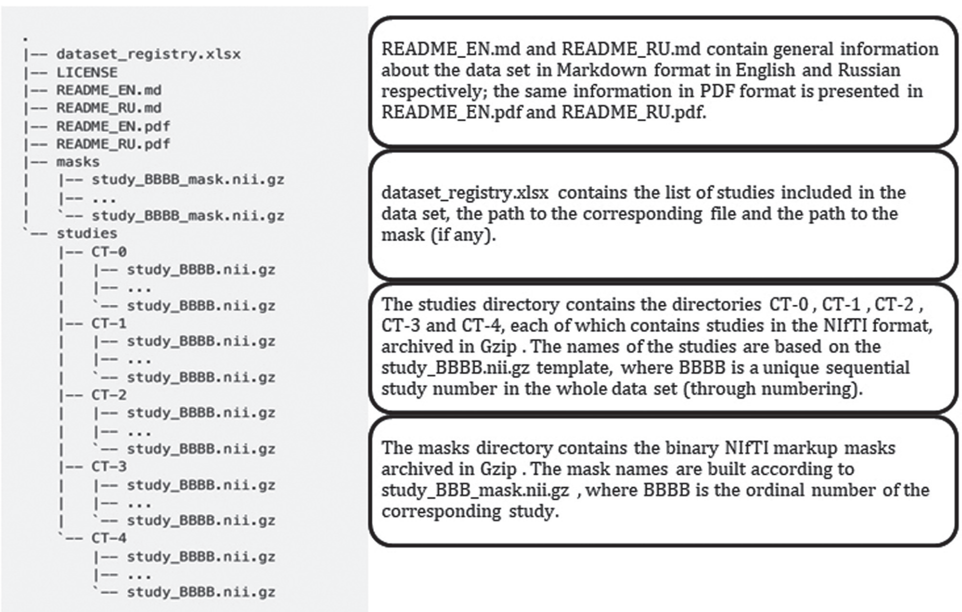

Figure 3: Data storage structure in the dataset.

ADDITIONAL INFO

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Conflict of interest. The authors declare no conflict of interest regarding this publication.

Authors contribution. S.P. Morozov — concept of research; A.E. Andreychenko — study design, data set formation; I.A. Blokhin — data markup, manuscript editing; P.B. Gelezhe — search for publications on the topic of the article, data markup; A.P. Gonchar — data markup, expert assessment of information; A.E. Nikolaev — data markup, expert assessment of information; N.A. Pavlov, V.Yu. Chernina, V.A. Gombolevsky — manuscript writing, preparing the dataset. All authors made a significant contribution to the study and preparation of the article, read and approved the final version before publication.

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МРТ лёгких беременной пациентки с пневмонией COVID-19

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В работе представлен клинический случай 39-летней беременной женщины с респираторными признаками новой коронавирусной инфекции COVID-19. Результаты исследования органов грудной клетки методом магнитно-резонансной томографии (МРТ) показали билатеральное поражение в базальных отделах. Тест на коронавирус методом полимеразной цепной реакции был положительным. Оценка состояния лёгких проведена без потери значимой диагностической информации. Кроме того, отсутствие воздействия ионизирующего излучения позволило избежать высокой дозовой нагрузки на пациентку и плод. Данный случай раскрывает перспективные возможности МРТ в диагностике лёгочной патологии без воздействия ионизирующего излучения, особенно в группах риска (дети, беременные и др.).

Ключевые слова: COVID-19; беременность; магнитно-резонансная томография; пневмония.

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Chest MRI of a pregnant woman with COVID-19 pneumonia

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This paper presents a clinical case of a 39-year-old pregnant woman with respiratory signs of the novel coronavirus Covid-19 infection. Chest MRI showed bilateral lesions in basal segments. The PCR test was positive. A lung condition was assessed without loss of significant diagnostic information. Besides that, the absence of exposure to ionizing radiation allowed to avoid a high loading dose on the patient and the fetus. This case reveals potential opportunities of MRI in the diagnosis of pulmonary pathology without exposure to ionizing radiation, especially in patient risk groups (children, pregnant women, etc.).

Keywords: COVID-19; pregnancy; magnetic resonance imaging; pneumonia.

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COVID-19
感染孕妇的肺部核磁共振成像

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本文报告介绍一例39岁孕妇临床表现为COVID-19呼吸体征的病例。胸部器官MRI显示双侧基底节病变。PCR检测结果阳性。在不丢失重要诊断信息的情况下对肺部状况进行评估。此外，非电离辐射使患者和胎儿避免大剂量辐射成为可能。本病例显示MRI在非电离辐射的情况下诊断肺病理，特别是在危险群体（儿童、孕妇等）。

关键词：COVID-19；妊娠；磁共振成像；肺炎

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INTRODUCTION

Diagnostic radiology of lung changes has become a part of the comprehensive medical evaluation of patients suspected with pneumonia caused by coronavirus disease 2019 (COVID-19). Since the method of choice is computed tomography (CT), visualization of the lungs in pregnant women raised significant difficulties. Notably, in Moscow, the average effective dose for a chest CT scan is 5.6 mSv [1]. Thus, a search for alternative non-ionizing methods led to performing magnetic resonance imaging (MRI) of the lungs.

CASE HISTORY

The patient was a 39-year-old woman at 26 weeks of gestation of her 4th pregnancy. The course of the pregnancy was satisfactory. She had no abortions and miscarriages. Previous pregnancies had no complications, which ended in birth of healthy children. Family history was unremarkable.

Epidemiological history: During her visit to the clinic, her husband and mother had manifestations of viral pneumonia. In July 2020, the patient came to the doctor with complaints of chest pain, body temperature up to 38.5°C, headache, and increased fatigue.

Physical examination: During auscultation, diminished vesicular breath sounds were heard, and crackles and wheezes were absent. Blood oxygen saturation based on pulse oximetry was 95%. During her visit, results of laboratory tests were unavailable. The result of the reverse-transcription polymerase chain reaction test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 RT-PCR) was positive obtained after MRI.

Given the epidemiological history and clinical manifestations suspicious for COVID-19 infection, imaging examination of chest organs is necessary to clarify the etiology of the disease. To avoid adverse effects due to exposure of the pregnant woman and the fetus to large radiation doses, chest MRI was performed. Personal protective equipment was used to ensure safety—surgical masks without ferromagnetic components—during the entire stay in the radiology department.

Initially, T2-weighted images (T2WI) were obtained in three planes using a single-shot fast spin echo (SSFSE) with the following parameters: repetition time (TR), 1300 ms; echo time (TE), 80 ms; flip angle, 90°; field of view (FOV), 450–450 mm; matrix, 512 × 512; slice thickness, 6 mm; spacing between slices, 6 mm; number of averages, 0.6; k-space filling method, Cartesian. These images were applied for planning axial FSE T2WI.

T1-weighted imaging was performed by LAVA 3D and IDEAL 3D. For LAVA 3D, the scanning parameters were as follows: TR, 4 ms; TE, 2.2 ms and 1.1 ms; flip angle, 10°; FOV, 400–400 mm; matrix 512 × 512; slice thickness, 3 mm; spacing between slices, 1.5 mm; number of averages, 0.7 with WATER and FAT fractions, in-phase/out-phase. For IDEAL 3D, the scanning parameters were as follows: TR, 5.8 ms; TE, 2.5 ms; flip angle, 3°; FOV, 440–440 mm; matrix, 256 × 256; slice thickness, 10 mm; spacing between slices, 10 mm; number of averages 0.7 with WATER and FAT fractions, in-phase/out-phase.

Diffusion-weighted imaging was performed by EPI pulse sequence with these parameters: TR, 10000 ms; TE, 62.3 ms; flip angle, 89°; FOV, 400–400 mm; matrix, 128×140; slice thickness, 5 mm; spacing between slices, 5 mm; number of averages, 1; b-values, 50,800 s/mm^2. The number of averages for SSFSE, LAVA-Flex, and EPI series was not higher than 1 to reduce blurring artifacts associated with the non-availability of respiratory gating. Free-breathing imaging study was conducted, a physical respiratory trigger was not used, but automatic synchronization was employed on the movement of the diaphragm to optimize the acquisition time.

The study was conducted in the supine position using abdominal and spinal radio frequency (RF) coils. The center of the abdominal coil was located in the middle of the sternum. To minimize dynamic artifacts associated with respiratory movements, the RF coil was fixed. The central laser beam was positioned at the mid-sternum.

Lung MRI was performed 7 days later, because the condition did not improve during treatment, and dry, ineffective cough worsened. MRI performed that time revealed zones of infiltration (Figs. 1, 2) in the lower lobes of the lungs.

DISCUSSION

In the present case, the diagnosis of SARS-CoV-2 infection was based on the epidemiological history, clinical manifestations, laboratory test results, chest CT findings, and a positive SARS-CoV-2 RT-PCR test result. All these methods are both useful and limited, as PCR test has a false-negative rate of at least 30%. Therefore, the diagnostic process should be complex [2]. The use of chest CT for COVID-19 screening is justified in patients with clinical and epidemiological suspicions, especially in cases with negative SARS-CoV-2 RT-PCR results [3].

The current pandemic has highlighted the importance of CT in the diagnosis and monitoring of COVID-19 pneumonia, as it is a more sensitive and effective method than X-ray. In addition, chest CT, including in pregnant women, contributes to early detection, severity assessment, and

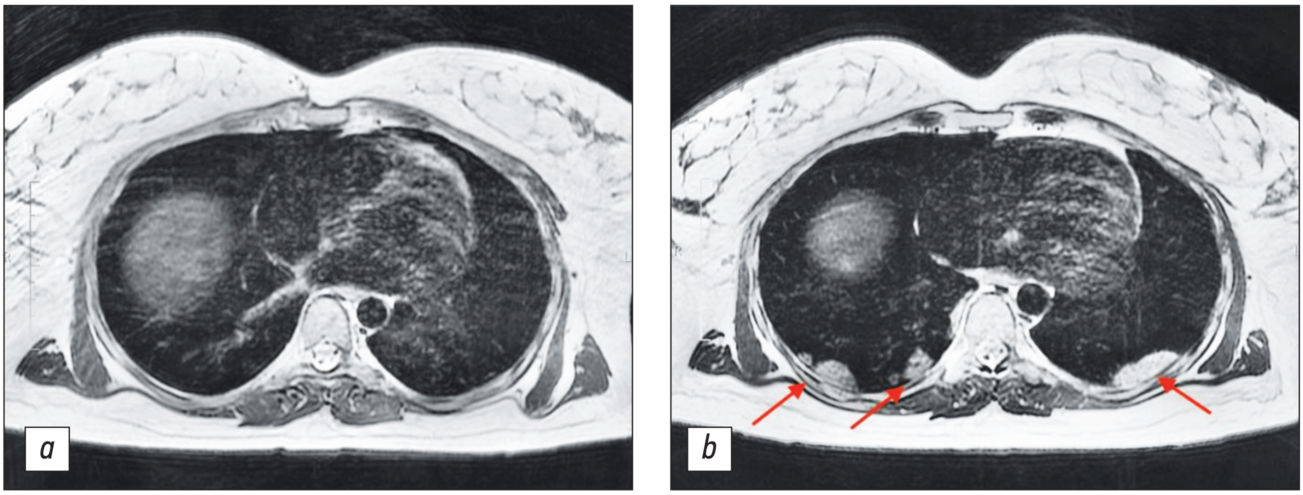

Figure 1. Chest magnetic resonance imaging, T2-weighted imaging single-shot fast spin echo: *a*) Primary examination, *b*) magnetic resonance imaging 7 days later. In Fig. 1b, consolidation zones in lower lungs appeared as areas of hyperintense and isointense signals.

monitoring of treatment effects to patients with or without confirmation of SARS-CoV-2 [4–5]. CT is associated with high patient radiation exposure. If a dynamic observation is required, the radiation load is increased accordingly [1].

This report presents a unique case of performing MRI of the lungs in a pregnant woman with COVID-19 pneumonia. Moreover, the case demonstrates the dynamic development of the disease according to MRI data. Notably, this is not the first case of performing chest MRI in pregnant women [6–11]. Kapdagli et al. reported on the detection of chondrosarcoma of the right lung by MRI in a 23-year-old pregnant woman. The tumor size was 18×16×17.5 cm^3, and it originated from the ribs [10]. Said et al. also described a rare case of primary lung liposarcoma diagnosed by MRI in a 28-year-old pregnant woman who complained of shortness of breath [11]. However, literature data on imaging of pregnant women with pneumonia caused by coronavirus infection were not available at the time of this writing. In this clinical case, the limitation was the inability to compare MRI and CT images. At present, no study has investigated MRI semiotics of COVID-19 pneumonia.

Currently, new pulse sequences, software, and modern technical equipment allow assessment of a lung condition using MRI [12]. Lung visualization is technically difficult due to the low density of the hydrogen protons in the lung parenchyma, as well as the rapid signal decay. However, pathological changes leading to tissue enlargement ("plus-tissue"), such as nodules, infiltrations, mucus, or pleural effusion, are easily detected with high diagnostic accuracy [14]. Although chest CT is more informative than MRI for detecting fine morphological structures, nowadays, MRI offers an increasing range of functional imaging techniques that surpass CT capabilities—perfusion, measurement of ventilation, and respiratory mechanics. Without a risk of exposing patients to ionizing radiation, repeated MRI examinations allow assessment of the disease course and quantitative monitoring of therapeutic response, providing a level of functional details that cannot

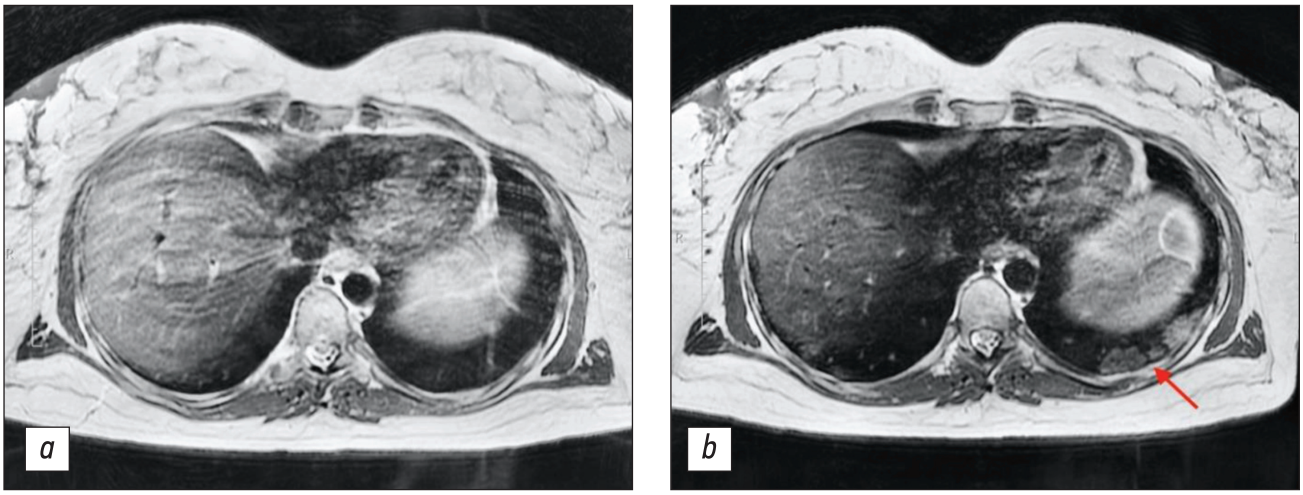

Figure 2. Chest magnetic resonance imaging, T2-weighted imaging single-shot fast spin echo: *a*) Primary examination, *b*) magnetic resonance imaging 7 days later. In Fig. 2b, consolidation zones in the lower right lung appeared as areas of hyperintense signal.

be obtained with any other imaging method [15, 16].

The data presented herein can be useful when performing MRI of other body parts, in particular MRI of the breast, thoracic spine, and abdominal cavity. For example, abdominal MRI can detect findings in the lower chest [8]. Identified changes can be overlooked or misinterpreted because of their location outside the main focus area of the study, as well as unawareness of how pathological changes in the chest organs look on MRI scans.

CONCLUSION

MRI can be used to detect changes in the lung in pregnant women with suspected COVID-19 pneumonia. Given its certain advantages, MRI of the lungs can be considered a method of choice in cases where dynamic monitoring is required. With the continuous improvement in software of scanners, chest MRI is a prospective direction for the development of diagnostic radiology in detecting pulmonary pathology.

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Профессор Анатолий Ильич Шехтер (18 января 1935 – 26 ноября 2020)

26 ноября 2020 г. нас постигла печальная весть — на 85-м году жизни после болезни скончался один из самых известных и уважаемых советских и российских рентгенологов профессор Анатолий Ильич Шехтер.

Десятки лет Анатолий Ильич нёс знания, свет и добро множеству поколений студентов и врачей. Его имя широко известно в нашей стране и за рубежом. Вся его жизнь с самого рождения была связана с медициной.

Professor Anatoly I. Shekhter (January 18, 1935 – November 26, 2020)

On November 26, 2020, a sad news befell us. One of the most famous and respected Soviet and Russian radiologists, Professor Anatoly I. Shekhter, died after an illness at the age of 85.

For decades, Anatoly Ilyich carried knowledge, light, and goodness to many generations of students and doctors. His name is widely known in our country and abroad. He associated his entire life with medicine.

https://doi.org/10.17816/DD54549

Anatoly Ilyich Shechter教授 (1935年1月18日—2020年11月26日)

在2020年11月26日，我们收到了一个悲伤的消息，苏联和俄罗斯最著名和最受尊敬的放射学家之一Anatoly Ilyich Shechter教授因病去世，享年85岁。

几十年来，Anatoly Ilyich为许多代学生和医生带来了知识以光明和善。他的名字在俄罗斯和国外都非常有名。他出生起就与医学有关。

Anatoly I. Shekhter was born in Dnepropetrovsk, Ukraine, 6 years before the war, into a family of doctors. His father, Ilya A. Shekhter (1907–1975), after the war, was a famous Soviet radiologist, doctor of medical sciences, professor, and honored master of sciences and engineering. He participated in the World War II and worked as the head of the evacuation hospital in Alma Ata (Kazakhstan). In 1943, the Shekhter family moved to Moscow. From 1954 to 1975, Professor I.A. Shekhter was the head of the Department of Rontgenology and Radiology of the N.A. Semashko Moscow Institute of Medicine and Dentistry, which was established by him. Following the family tradition, the younger brother of Anatoly I. Shekhter, Yuri I. Shekhter, also became a famous Russian radiologist.

Professor I.A. Shekhter also influenced the choice of life path of his eldest son, and in 1958, Anatoly I. Shekhter graduated from the Second Moscow State Medical Institute (now the N.I. Pirogov Russian National Research Medical University). The medical biography of the graduate, like many young specialists of that time, started with the work of a general practitioner in the virgin lands, in Kazakhstan. Upon his return to Moscow in 1964, Anatoly I. Shekhter entered the Department of Radiation Diagnostics and Therapy (Roentgenology and Radiology) of the I.M. Sechenov First Moscow State Medical Institute (now the Sechenov University), where he worked until his last day. Most of his life was inextricably linked with the university and his favorite department.

For many years, radiation diagnostics of respiratory diseases has become one of the main fields of the scientific and teaching activities of Anatoly I. Shekhter. In 1964, he defended his Ph.D. thesis on the clinical and radiological diagnosis of lung lesions. In 1972, he defended his doctorate thesis with the topic of radiation diagnosis of chronic inflammatory diseases of the lungs. Since 1975, Anatoly I. Shekhter started to study a new scientific topic, radiation diagnostics of diseases of the mammary glands. In 1980, he was awarded the title of "Professor."

For decades, the teaching and scientific work of Anatoly I. Shekhter was performed in close cooperation with the famous heads of the legendary Department of Radiation Diagnostics and Therapy of First Medical Institute, Professors Leonid D. Lindenbraten and Leonid A. Yudin and Academician Sergei K. Ternov.

Professor Anatoly I. Shekhter was one of the most outstanding and most famous professors of the department. He is an author of hundreds of scientific articles and co-author of three monographs and a textbook, as well as several educational materials. A total of 16 Ph.D. theses were prepared under his supervision.

For his active and fruitful work, Professor A.I. Schechter was awarded many prizes, namely, the medal For the Development of Virgin Lands in 1958, the badge Excellent Worker of Public Health in 1970, and the medal Veteran of Labor in 1980. In 2008, Anatoly I. Shekhter became a laureate of the Professor Yu.N. Sokolov badge of honor.

Anatoly I. Shekhter was a highly cultured man. He was famous with his professionalism, benevolence, optimism, and desire to help young colleagues. He was loved and respected by students, residents, graduate students, and colleagues of the department.

In addition to medicine, Anatoly I. Shekhter knew literature, poetry, and remembered and recited hundreds of poems by heart. Some of his favorites were the lines from the famous poem by Boris Pasternak:

"In everything, I want to reach
For the very essence.
In work, in searching for the path,
In the heart's turmoil.

For the essence of days gone by,
For their causes,
For foundations, for roots,
For the core.

I want to live, to think, to feel, to love,
To make discoveries
Always grasping the thread
Of fates and events"

He is retained in our memory. The cherished memory of Professor Anatoly I. Shekhter will always dwell in our hearts.

On behalf of the Russian Society of Rontgenologists and Radiologists (RSRR) and the Moscow Society of Radiologists of RSRR (MSR RSRR) V.E. Sinitsyn, S.P. Morozov